

FIG. 1

SYNTHETIC COMBINATORIAL ANTIBODY LIBRARY

Achim KNAPPIK et al. PROTEIN/ (POLY) PEPTIDE LIBRARIES Application No. 09/490,324

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F/G. 2A

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FIG. 2C

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FIG. 2D

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| | I | \$ C C T | Ε | 7 | S | 9 | L | 8 | 6 | O T | TT | IZ | 13 | ÐΤ | SI | 9 T | LI | 8 T | 6 T | 20 | ZI | 22 | 23 | 52 | 25 | 26 | 72 | 82 | 62 | 3 0 |
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FIG. 2E

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| |] 98 | L 28 | 88 | 68 88 48 98 | 06 | 16 | 26 | 83 | ₹ 6 | 96 | 96 | ۷6 | 86 | 66 | 001 | A | B | ้อ | TOT | TOS | EOI | DO T | SOT | 901 | 70T | 60T | OII | | IIS | EII |
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FIG. 2F

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F/G. 2G

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| S BanI | GAG CCC CTC GGG | H K | } | P G SexAI | } | رن ن | |
| д С | ~ AGA ICT | C PstI | √~~ IGC ACG | | ACC TGG | Ω | 0 0 0 0 0 |
| O) | CC2 | [[| \(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\frac{1}{2}\)\(\fr | Q X | AAA | ο λ | AAA(TTT |
| H | TGACCCAGAG ACTGGGTCTC | H | ATTACCTGCA TAATGGACGT | Q | GCAGAAACCA CGTCTTTGGT | O. | TGCAAAGCGG ACGTTTCGCC |
| Z | | | | O ² | | Ы | |
| \circ | CAG | H | SAC TTG | | √~~ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | Ŋ | 4GC |
| I RV | TCC | \triangleright | 'GTC | / Y KpnI | GGTACC CCATGG | W | 1,007. |
| .D I ECORV | ~~~~~ GATATCCAGA CTATAGGTCT | 民 | TCGTGTGACC AGCACACTGG | _ | CGTGGTACCA GCACCATGGT | Æ | GCCAGCAGCT CGGTCGTCGA |
| • | ひじ | | HA | \forall | OQ | | Ω |

FIG. 3A

| P E D F Eco57I | BbsI ~~~~~~ GAAGACTTTG CTTCTGAAAC | F G Q MscI | CTTTGGCCAG GAAACCGGTC | | |
|--------------------|------------------------------------------------|---------------|------------------------------------------------|------------|-----------------------------------------------------------------------------------------------|
| S S L Q P E ECO57I | CCATTAGCAG CCTGCAACCT GGTAATCGTC GGACGTTGGA | T T T T T | CATTATACCA CCCCGCCGAC GTAATATGGT GGGGCGGCTG | T .WI | ებე დენ |
| Н | CCATT GGTAA | Х Н | CATTA GTAAT | 形 BS 1. | $\widetilde{\mathbb{A}} \widetilde{\mathbb{A}} \widetilde{\mathbb{A}} \widetilde{\mathbb{A}}$ |
| T L T | CTGA GACT | О О | GCAG | M H | TTAA AATT |
| E E | TTTACCCTGA | O U | TTGCCAGCAG AACGGTCGTC | 団 | TTGAAATTAA AACTTTAATT |
| Q L D | BamHI CGGCACTGAT I GCCGTGACTA A | X X L | CGACCTATTA I GCTGGATAAT A | T K V | GGTACGAAAG 1 CCATGCTTTC A |
| . | Bar ~ CG(| A | G G G | D | 0 0 0 0 |

FIG. 3B

口 GAGGCCCGCT CATAGCAACG GTATCGTTGC AAGCCCGCAG TTCGGGCGTC CTGCCAGTGA CTCCGGGCGA \bigcirc ${\mathbb Z}$ \mathcal{O} Д ഗ Д S 出 \vdash GACGGTCACT AAGCCTGCTG AACCAGGTCA TTGGTCCAGT TTCGGACGAC Ø 口 > ~~~~~~ Ç SexAI 口 Д Д ഗ 口 又 GAAGCAGCCA CTTCGTCGGT TGACCCAGAG CCCACTGAGC ACTGGGTCTC GGGTGACTCG AGACCTAACC ATGGAAGTTT TCTGGATTGG TACCTTCAAA O ഗ Ø ഗ 口 口 ഗ Д ~~~~~ KpnI BanI. α TAATCGACGT ATTAGCTGCA PstI Ŋ 2 \mathcal{O} O Ω ഗ Н П \succeq CTATAGCACT GCTATAACTA GATATCGTGA CGATATTGAT GCCTGCGAGC CGGACGCTCG \succ ഗ Z K ECORV ~ ~ ~ ~ ~ ~ ~ × Д C

FIG. 3C

| о В В | CGGATCGTTT GCCTAGCAAA | ಬ ಸ > | AGCCGTGTGG TCGGCACACC | E E | TACCACCCCG ATGGTGGGGC |
|------------------|------------------------------------------------|------------------------|------------------------------------------------|-------------------------------------|------------------------------------------------|
| S G V P SanDI | AGTGGGGTCC TCACCCCAGG | J K | CCTGAAAATT GGACTTTTAA | О Н У | AGCAGCATTA TCGTCGTAAT |
| Y L G S N R A | ATCTGGGCAG CAACCGTGCC TAGACCCGTC GTTGGCACGG | G S G T D F T Bamhi | GGATCCGGCA CCGATTTTAC CCTAGGCCGT GGCTAAAATG | V G V Y Y C Q | CGTGGGCGTG TATTATTGCC GCACCCGCAC ATAATAACGG |
| L L I Asel | СТАТТААТТТ GATAATTAAA | დ დ | TAGCGGCTCT ATCGCCGAGA | E A E D ECO57I ~~~~~~ BbsI | AAGCTGAAGA TTCGACTTCT |

FIG. 3D

BsiWI 召 X 口 \bowtie CGGTCCCATG \vdash \mathcal{O} MscI ſщ \vdash Д

FIG. 3E

| 闩 | GA | | TC | ≯ |
|--------------------------------------|------------------------------------------------|----------------------|-------------------------------------------------------------------------------------|---------------------------------------------------|
| L T Q S P A T L S L S P G E Banii | TGACCCAGAG CCCGGCGACC CTGAGCCTGT CTCCGGGCGA | LSCRASQSVSSY Psti | CTGAGCTGCA GAGCGAGCGTGAGC AGCAGCTATC GACTCGACGT CTCGCTCGGT CTCGCACTCG TCGTCGATAG | L A W Y Q Q K P G Q A P R L L I Y KpnI SexAI AseI |
| Д | 999 | Ŋ | AG(| L L AseI |
| | CTC | W | AGC ICG | AS ~~~ |
| W | T. A. | | ပ္ပုတ္ | ь |
| 니 | CTG | O) | GAG | \simeq |
| W | 18C(| \triangleright | GT(| |
| c | IGA ACI | Ø | AGC ICG | 14 |
| | 56 | | ĞAGCGAGCCA GAGCGTGAGC CTCGCTCGGT CTCGCACTCG | A. |
| \vdash | ACC | O. | CC2 GG1 | O. |
| A. | 0 0 0 0 | Ω | 3AG UTC | ۲h ك > |
| Д | ~ GGG GCG | A | 000 | P G SexAI |
| ΙΙτ | ~ C C C C C C C C C C C C C C C C C C C | ~ | Ç GA CTI | о С С С С |
| S Banii | TGACCCAGAG CCCGGCGACC ACTGGGTCTC GGGCCGCTGG | C B PstI | ~~~~~~ CTGCA G GACGT C | ⋈ |
| \circ | CAG GTC | Д В | CTGAGCTGCA GACTCGACGT | O . |
| \vdash |) (0 (0 (0 | W | HAG(| 0 |
| | IGA ACT | ᆸ | CTG | ~ |
| 니 | | Γ. | ပ္ပုပ္ပု | W Y KpnI ~~~~~~ |
| \triangleright | GATATCGTGC CTATAGCACG | R A T | ACGTGCGACC TGCACGCTGG | W KK |
| D I EcoRV | YTC YTC | Ø | 7GC 1CG | √ ¹ |
| й Н | ~~~~~ GATATC CTATAG | 民 | CG. | 7 |
| | ≀ ଫ ଠ | | A H | 긔 |
| | | | | |

FIG. 3F

| CCAGCAGAAA CCAGGTCAAG CACCGCGTCT ATTAATTTAT GGTCGTCTTT GGTCCAGTTC GTGGCGCAGA TAATTAAATA | A R F S G S G Bamhi | ? | GCGCGTTTTA GCGGCTCTGG | CGCCGAGACC | P E D Eco57I | <pre></pre> | BbsI | <pre></pre> | CCTGAAGACT | GGACTTCTGA |
|--------------------------------------------------------------------------------------------|------------------------|----------------------|-----------------------|---------------|-----------------|-------------|-------|--------------|-----------------------|-----------------------|
| GTCT CAGA | <u>г</u> ч | | TTTA | CGCGCAAAAT | വ വ വ | | | | GGAA | CCTT |
|) (G) (G) (G) | ద | | GT | ₹ | 口 | | | | CT | GGA |
| CACC | Æ | | GCGC | | ഗ | | | | CAG(| GTC |
| AG TC | Д | ? | 000 | <u>ر</u> و | ഗ | | | | AG | TC |
| TCA AGI | SanDI | ≀ ≀ | TCC | AGG | Н | | | | ATT | TAZ |
| CCAGGTCAAG GGTCCAGTTC | G V P SanDI | <pre></pre> | TGGGGTCCCG | ACCCAGGGC | D F T L T I S | | | | TGACCATTAG CAGCCTGGAA | ACTGGTAATC GTCGGACCTT |
| A.A. | H | | | | H | | | | | |
| GAZ CTJ | ø | | CAZ | <u>.</u> | E-4 | | | | JAC(| \TG(|
| GCA | ద | | GTG | CAC | Гщ | | | | TT | AAZ |
| CCAGCAGAAA GGTCGTCTTT | S R T | | GCCGTGCAAC | CGGCACGI"I'G | Ω | | | | GATTTTACCC | CTAAAATGGG |
| GTA | | | GCA |)) | [- - | | | | ACG | TGC |
| GTG CAC | Ø | | CGA | | <u>ග</u> | | Н | | 999 | SSS |
| TGGCGTGGTA ACCGCACCAT | S S | | GGCGCGAGCA | | ഗ | | BamHI | ? ? ? | ATCCGGCACG | TAGGCCGTGC |
| | | | | | | | | | | |

FIG. 3G

| F A V Y | × | × | Ö | Ø | Ø | 田 | \succ | ⊱ | ⊣ | Д | Д | Y C Q Q H Y T T P P T F G | Ľτί | Ŋ |
|------------|----|-----------------------|-------|-------------|-----------------------|----------|---------------------------------------|-----|------------|---------------|---------------|---------------------------|------|---------------------------------------|
| | | | | | | | | | | | | | Ï | MSCI |
| | | | | | | | | | | | | | ì | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ |
| TTGCGGTGTA | Ą. | TTATTGCCAG | TGC | | CAGCATTATA CCACCCCGCC | CAT | TATA | Ŭ | CACC | CCG | \mathcal{C} | GACCTTTGGC | rTT(| 3GC |
| AACGCCACAT | Ę | AATAACGGTC | ACG | GTC | GTC | 3TA | GTCGTAATAT | | GGTGGGGCGG |) B | (J) | CTGGAAACCG | 1AA(| |
| E O | X | K V E I | Ы | | X X | 民 | ₽. | | | | | | | |
| MscI | | | | | | Щ | BsiWI | , , | | | | | | |
| | | | | | | ? | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | , | | | | | | |
| CAGGGTACGA | | AAGTTGAAAT TAAACGTACG | TGA | AAT | TAA | ₹CG | TACG | z b | | | | | | |
| 上して日くしてした | | | F C K | K E K | י די די ל | 7 | 7 | , | | | | | | |

FIG. 3H

| 臼 | CGA GCT | Ø | GCA CGT | Ω ₄ | 0 0 0 0 |
|------------------|------------------------------------------------|----------------|------------------------------------------------|-----------------|------------------------------------------------|
| O | 36G(| | CAC | വ |) 1000 |
| H | GCCTGGGCGA CGGACCCGCT | Ω | TATAGCAGCA | O | ~ TCAGCCGCCG AGTCGGCGGC |
| S | | <i>P</i> 1 | | | ~~ T(A)(|
| > | CTGGCGGTGA | Ы | GAGCGTGCTG | P G SexAI | AGAAACCAGG TCAGCCGCCG TCTTTGGTCC AGTCGGCGGC |
| K | - CGC | \gt | GTG | አ ማ ያ | ACC TGC |
| ьì | TGG ACC | ഗ | AGC TCG | × | GAA CTT |
| | | \bigcirc | | O | |
| W | AGO | Q | CC2 GG3 | Q | AG(TC(|
| О | SAT | Ŋ | CAG | 7 T T | √~~ \ GG |
| Д | CCCGGATAGC | Ŋ | ~ GAAGCAGCCA CTTCGTCGGT | W Y Q Q KpnI | ~~~~~~ TGGTACCAGC ACCATGGTCG |
| S BanII | AG CCC TC GGG | 凶 | GA CT | Ŋ | TG AC |
| S Bal | TGACCCAGAG CCCGGATAGC ACTGGGTCTC GGGCCTATCG | C B PstI | ATTAACTGCA GAAGCAGCCA TAATTGACGT CTTCGTCGGT | A. | 0 0 0 0 |
| Q | CAG GTG | | ~~~ CTG GAC | ц | TGG ACC |
| [-1 . |) () () () () | Z | AA! | П | ATC. |
| | TGA ACI | Н | ATTAACTGCA TAATTGACGT | ≯ | CTATCTGGCG GATAGACCGC |
| V M | | c . | | Z | |
| | GTG | [| GAC | N N | AA <i>2</i> TTT |
| I ORV | √~~ ATC PAG | Þ | rgc Acg | Z | ACA PGT |
| D I EcoRV | ~~~~~ GATATCGTGA CTATAGCACT | 召 | ACGTGCGACC TGCACGCTGG | z Z | ACAACAAAAA TGTTGTTTTT |
| | ≀ დ ბ | | 4 H | Z | K H |

| 民 | | 0 0 0 0 | |) () () () | E | | | • |
|------------|---------------------------------------|--------------------------------------------------------------------------------------------------|--------------|---------------------------|------------------|------------|------|---------------------------------------|
| Ω | | ATCCACCCGT GAAAGCGGGG TCCCGGATCG TAGGTGGGCA CTTTCGCCCC AGGGCCTAGC | Ŋ | ATTTCGTCCC TAAAGCAGGG | [- - | | | |
| Д | } |) 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | Ŋ | TC | | | | |
| | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | TCC | Н | ATT TAZ | ≯ | | | |
| V SanDI | } | (h) (h) | F | TACCCTGACC ATGGGACTGG | 耳 | | | |
| U T | } | 900 | I I | GA(| O ₄ | | | |
| W | | AGC ICG | | CCI | o o | | | • |
| ы | | AAA YTT | H | PAC. | | | | |
| | | | ſъ | | Ŋ | | | |
| 民 | | TTTATTGGGC ATCCACCCGT AAATAACCCG TAGGTGGGCA | Д Н | GCACTGATTT CGTGACTAAA | X X | | | |
| \vdash | | ACC TGC | | TG | \Rightarrow | | | |
| W | | TCC | H | CAC | \triangleright | | | |
| A . | | A Ei | Ŋ | | | | | |
| Y W A | | TTTATTGGGC AAATAACCCG | S H | TCTGGATCCG AGACCTAGGC | Ø | | | |
| M | | rtg AAC | G S BamHI | ~~~~~ GGATCC CCTAGG | \gt | | | |
| ≯ I | | TAT | | ŽHG. | Д | , | ш | } |
| Н | } | | Ø | | 7 I | ? | BbsI | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ |
| L AseI | <pre></pre> | raa att | O | 0 0 0 0 | A E Eco57I | ? ? | Д | ? |
| | ? | AT. | S |) (CG(| αщ | ξ | | |
| X L | | АААСТАТТАА ТТТGАТААТТ | · Ľų | TTTTAGCGGC AAAATCGCCG | O | | | |
| X | | AA T'T' | • • | TT | ü | | | |
| | | | | | | | | |

FIG. 3J

GCCAGCAGCA TTATACCACC CGGTCGTCGT AATATGGTGG GAAATTAAAC GTACG CTTTAATTTG CATGC BsiWI 召 × Н 闰 TACGAAAGTT GGCGGCTGGA AACCGGTCCC ATGCTTTCAA TGCAAGCTGA AGACGTGGCG GTGTATTATT CACATAATAA X \vdash ACGITCGACT ICTGCACCGC CCGCCGACCT TTGGCCAGGG Ċ O MscI Ċ ш \vdash Д Д

FIG. 3K

AGTGGCGCAC CAGGTCAGCG CAACATTGGC AGCAACTATG GCTGATTTAT α TCGTTGATAC TCACCGCGTG GTCCAGTCGC Q Z C 口 SexAI ഗ Д CCCGGGACGG CGCCGAAACT GTTGTAACCG 口 C K X Н \mathcal{O} Д \geq S BbeI Þ GCAGCAGCAG CGTCGTCGTC GCCTTCAGTG CGGAAGTCAC ഗ \gt \vdash Eco57I ~~~~~ S S ~~~~~ Ç XmaI S Д Д C TGTGACCATC TCGTGTAGCG GICTCGCACG ACTGGGTCGG ACACTGGTAG AGCACATCGC TGACCCAGCC TGAGCTGGTA CCAGCAGTTG Д 口 S \bigcirc Ø BSSSI \vdash Ø S KpnI П CAGAGCGTGC H2 \vdash S ഗ \gt Ø \gt

FIG. 4A

CGACTAAATA

GGGCCCTGCC GCGGCTTTGA

ACTCGACCAT GGTCGTCAAC

Achim KNAPPIK et al. PROTEIN/ (POLY) PEPTIDE LIBRARIES Application No. 09/490,324

¥ ACACAAACCG CGCCTAGGTT AGCGAAGACG TCGCTTCTGC GCGGATCCAA BbsI BamHI S 口 \mathcal{O} ഗ S GTCGTAATAT GGTGGGGCGG CTAGCAAAAT AGCGCGAGCC TTGCGATTAC GGGCCTGCAA TCGCGCTCGG AACGCTAATG CCCGGACGTT GATCGTTTTA Ø ഥ щ \Box 召 Ç H AGCGTCCCTC AGGCGTGCCG CTATTGTTGG TCGCAGGGAG TCCGCACGGC CAGCATTATA \vdash Д \triangleright 口 Þ C Bsu36I \Box AATAACGGTC Y C Q TTATTGCCAG S S Д Þ 召 S Ø GATAACAACC AAGCGGCACC TTCGCCGTGG TTCGCCTAAT AAGCGGATTA Z Д C Z Ø ഗ Д 口

FIG. 4B

| C |
|----|
| 4 |
| G. |
| F |

GGCGCCACGA AGTTAACCGT TCTTGGC CCGCCGTGCT TCAATTGGCA AGAACCG

HpaI

×

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ഗ AGCGGCTCAC CAGGTCAGAG CCGATATTGA GGCTATAACT TGACTACTAA GTCCAGTCTC ACTGATGATT Н Z Ø Ξ C 口 SexAI Ç Д AGGCGCCGAA TCGCCGAGTG CGATGTGGGC GCTACACCCG × Ç ഗ Д BbeI C Ø \Box S 又 GTACTAGCAG CATGATCGTC CATCCCGGGA AGCTTCAGTG TCGAAGTCAC Eco57I ഗ \gt Ç XmaI ~ ~ ~ ~ ~ ~ ~ ഗ S Д \vdash K 工 C AGCACATGCC GTACCAGCAG TGACCCAGCC TCGTGTACGG ACTGGGTCGG Д O \vdash Ø Ø S C BssSI \vdash KpnI \succ 口 ATGTGAGCTG GTAATGGTAG CAGAGCGCAC CATTACCATC GTCTCGCGTG 3 HÞ S \vdash S > \mathbf{H} Ø >

FIG. 41

TCCGCGGCTT

GTAGGGCCCT

CATGGTCGTC

TACACTCGAC

| SH. | 7 L | H > | 7G | ſτ. | L'T A.A |
|----------------------------|------------------------------------------------|---------------------------------|---------------------------------------------------------------------------------------------|------------------|--------------------------|
| S G S BamHI | TTAGCGGATC AATCGCCTAG | E E E E E E E | GCCTGACCAT TAGCGGCCTG CAAGCGGAAG CGGACTGGTA ATCGCCGGAC GTTCGCCTTC | YYC QQHY TTPPVF | GCCTGTGTTT CGGACACAAA |
| Д ≀ | 9 9 9 9 | K | 0 0 0 0 | \triangleright | IGT ACA |
| Οĵ | TAG | NTASLTISGLOAE Bb | AAG TTC | വ | CCJ GGZ |
| Ĺτι | | | ت ن | | |
| ~ | TT: | ᆸ | CTG 3AC | Щ | 7CC |
| 114 |) 000 | Ch | 999 | [- 1 | AC(TG(|
| Z | AA TT | | Ω Ω Ω | ⊱ |)) () |
| W | AGCAACCGTT TCGTTGGCAA | O) | TAGCGGCCTG ATCGCCGGAC | | ATACCACCCC TATGGTGGGG |
| | | Н | | ≻ | |
| \wedge | GT | . | GCCTGACCAT CGGACTGGTA | 出 | CAGCAGCATT GTCGTCGTAA |
| ტ } | 3 3 3 3 3 3 3 3 | H | 3AC CTG | \bigcirc | AGC |
| P S G Bsu36I | CA(GT(| 니 | CTC | <u> </u> | GG. |
| P S Bsu36I ~~~~~~~ | CT GA | 7.0 | 9 9 | O | CA |
| N R P S G V S N R F Bsu36I | GCAACCGTCC CTCAGGCGTG CGTTGGCAGG GAGTCCGCAC | 01 | GA | ر ا | G G G |
| K | GT | Ø | ς Ο Ο Ο | | TT |
| b | 100 100 | \vdash | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | Я | LT7 PAT |
| 4 | CA/ | Z | AACACCGCGA TTGTGGCGCT | ⊱ | TTATTATTGC AATAATAACG |
| വ | | | | | |
| | rga act | <u></u> ტ . | 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 | Н | 3G2 |
| | TG. AC. | S |) (3) | A. |) (CG) |
| A D A | JGA CT | Z HH | AAA TTT: | 田田 | BAA TTT |
| \succ | TATGATGTGA ATACTACACT | K BamHI ~ | CAAAAGCGGC GTTTTCGCCG | D E BbsI | ACGAAGCGGA TGCTTCGCCT |
| | | , , , | | | |

FIG. 4E

| | L | |
|------------|------------------------------|--------|
| GCAAGAACCG | GCTTCAATTG | CGCCGT |
| CGTTCTTGGC | GCGGCA CGAAGTTAAC CGTTCTTGGC | GCGGCA |
| ? ? ? | ~ ~ ~ ~ ~ | |
| MscI | HpaI | |

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 \mathcal{O}

FIG. 4F

| T Q P P S V S V A P G Q T SexAI | CC GCCTTCAGTG AGCGTTGCAC CAGGTCAGAC GG CGGAAGTCAC TCGCAACGTG GTCCAGTCTG | S G D A L G D K Y A S | CG GCGATGCGCT GGGCGATAAA TACGCGAGCT GC CGCTACGCGA CCCGCTATTT ATGCGCTCGA | KPGQAPVLVIYDD |
|---------------------------------|-------------------------------------------------------------------------|-----------------------|----------------------------------------------------------------------------|---------------|
| വ | | ڻ ت | | Ŋ |
| CV EH | TGACCCAGCC ACTGGGTCGG | S C S BSSSI | TCGTGTAGCG AGCACATCGC | 저 면 |
| 자 표 고 | AGCTATGAAC TG TCGATACTTG AC | A R I Bs | CGCGCGTATC TC GCGCGCATAG AC | M Y Q Q |
| Ω ≻i | AGCJ TCG2 | K. | 00C(| M |

F/G. 4G

TTATGATGAT AATACTACTA TTCTGGTGAT AAGACCACTA CAGGCGCCAG GTCCGCGGTC GAAACCCGGG CTTTGGGCCC GGTACCAGCA CCATGGTCGT

Ċ GGTTGTCGCC ഗ Z BamHI ~~~~~ ഗ TTTAGCGGAT AAATCGCCTA Ċ ഗ ſΉ GGGCCTTGCG 召 口 Д GGAGTCCGTA CCTCAGGCAT Ç ~~~~~~ Bsu36I S Д AGACTGGCAG TCTGACCGTC 召 \Box S

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FIG. 4H

GACGAAGCGG CTGCTTCGCC ACCGCCGCCG TGGCGGCGGC TTAGCGGCAC TCAGGCGGAA AATCGCCGTG AGTCCGCCTT TATACCACCC CGCCTGTGTT ATATGGTGGG GCGGACACAA \vdash CAACACCGCG ACCCTGACCA TAATAATAAC GGTCGTCGTA TGGGACTGGT D Y Y C Q Q H ATTATTATTG CCAGCAGCAT GTTGTGGCGC

T K L T V L G Hpai MscI ACGAAGTTAA CCGTTCTTGG C TGCTTCAATT GGCAAGAACC G FIG. 41

| ഗ | <i>የ</i> ካ የ ነ | | d F1 | | ር) የካ |
|------------------|--------------------------------|------------------|---------------------------|------------------------|------------------------------------------------------------------------------------------------------------------|
| 01 | CA(| ₫'. | 100 1007 | Ŋ | 000 |
| W | AG(TC(| . 4 | TG AC | | $\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}\mathcal{C}$ |
| Ŋ | CGGGCAGCAG GCCCGTCGTC | X X | AGCTATGCGA TCGATACGCT | M G | GATGGGCGGC CTACCCGCCG |
| | 99 | S |) (G | Ξ | AT. |
| Д | | | • | h-> | |
| \ | AAC 7TG | ഗ | \GC | M | STG CAC |
| V K K P | GTGAAAAAAC CACTTTTTTG | E F | CACTTTTAGC GTGAAAATCG | 田田田 | GTCTCGAGTG CAGAGCTCAC |
| K | AAZ I'T'I | 1-4 | I'T'I AAZ | L XhoI | ~~. HC(AG(|
| > | TG. | E | AC, TG, | | TC' AG. |
| r | | | | CD | |
| 田 | TGGCGCGGAA ACCGCGCCTT | Ç | CCTCCGGAGG GGAGGCCTCC | <u> </u> | CCTGGGCAGG |
| G B E | 0 0 0 0 0 | S G BspEI | ~~~~~ TCCGGA AGGCCT | O | 3CA 3GT |
| A. | 000 | 3.5.D | | CD | |
| Ċ | 200 | 07 дд | ZTC GAC | வ | ~ ~ ~ CTC GAC |
| | T(A(| ₫. | | _ X | ì ŏ ŏ ≥ |
| W | TC AG | CK | AGCTGCAAAG TCGACGTTTC | R Q A P G Q G BstXI | GCGCCAAGCC CCTGG CGCGGTTCGG GGACC |
| S | ~~ TGGTTCAGTC ACCAAGTCAG | × | AGCTGCAAAG TCGACGTTTC | Щ | ~~ AG 'TC |
| _ | TT. | \mathcal{O} | 09. 00. 00. | O | 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 |
| \triangleright |) (C.) | Ŋ | CG2 | K | |
| ДΗ | | 01 | A(| | \mathcal{G} \mathcal{G} |
| Q MfeI | ~~~~ AAT TTA | \triangleright | A A C | \triangleright | GT |
| QΞ | ~ CA Z | • | AG' TC | M | φ Ο Ο |
| \triangleright | CAGGTGCAAT GTCCACGTTA | V K V | CGTGAAAGTG GCACTTTCAC | M | TTAGCTGGGT AATCGACCCA |
| > ŏ | , 20 20 | > | TG AC | വ | AG TC |
| O | CA GT | | 90 | H | TT AA |
| | | | | | |

FIG. 5A

TAATAACGCG CGCAACCCCG TACCTTGACT ATTATTGCGC GCGTTGGGGC CGCGTCTTCA AAGTCCCGGC G 口 3 口 α Ξ Щ BSSHI CACCGCGTAT GTGGCGCATA K \mathcal{O} K \vdash CCGCTTGATG AAAGCACCAG TTTCGTGGTC ACGGCCGTGT ATCGCTTCTA TGCCGGCACA ഗ \vdash ~~~~~ EagI Q ഗ \vdash 口 TAATAAGGCT AAAAACCGTG ACCGCGGATG TGGCGCCTAC TAGCGAAGAT \Box 口 Þ S Н GGTGACCATT CCACTGGTAA GCAGCCTGCG CGTCGGACGC 召 Н Д 口 ~~~~~ BStEII ഗ ഗ

FIG. 5B

 \vdash

CCCTGGTGAC GGGACCACTG Н CCGGTTCCGT GGCCAAGGCA \mathcal{Q} StyIØ O GGATTATTGG 3 \triangleright \Box GGCGATGGCT TTTATGCGAT CCGCTACCGA AAATACGCTA Ξ K \triangleright GGTTAGCTCA G CCAATCGAGT C ſτι BlpI G ഗ \Box \gt G

TCGATAATAT GATGGGCTGG CTACCCGACC S GCCGCGCTC AGCTATTATA \geq Ø Ç \mathcal{O} Ξ ഗ Д GTCTCGAGTG CACTTTTTG ATGGAAATGG CAGAGCTCAC TACCTTTACC 3 GTGAAAAAAC \vdash X L E XhoI Ľ X \vdash \mathcal{O} GGCGGTTCGG GGACCCGTCC CCTCCGGATA CCGCCAAGCC CCTGGGCAGG GGAGGCCTAT CGGCGCGGAA GCCGCGCCTT × 口 BSpEI Q Ç Þ \mathcal{O} S Ċ Д BstXI K GICCACGITA ACCAAGICIC AGCTGCAAAG CAGGTGCAAT TGGTTCAGAG TCGACGTTTC ഗ Ø × Ø Ø \mathcal{O} 召 ഗ ~~~~~ Q L MfeI TGCACTGGGT CGTGAAAGTG GCACTTTCAC ACGTGACCCA \gt \geq 工 \triangleright Ø Ξ

FIG. 5D

A Q K F Q G R GCGCAGAAGT TTCAGGGCCG CGCGTCTTCA AAGTCCCGGC I N P N S G G T N Y ATTAACCCGA ATAGCGGCGG CACGAACTAC TAATTGGGCT TATCGCCGCC GTGCTTGATG

4

CACCGCGTAT ATGGAACTGA GTGGCGCATA TACCTTGACT П 口 \boxtimes K \vdash CCAGCATTAG GGTCGTAATC S ഗ \vdash ACCCGTGATA TGGGCACTAT \Box K H GGTGACCATG CCACTGGTAC Ξ V T BstEII ~~~~~

C 3 召 BSSHII \gt EagI Ø \vdash Д 口 ഗ 召 口 S S

~ ~ ~ ~ ~ ~

TAATAACGCG CGCAACCCCG ATTATIGCGC GCGTIGGGGC ATCGCTTCTA TGCCGGCACA ACGCCCGTGT TAGCGAAGAT GCAGCCTGCG CGTCGGACGC

FIG. 5E

 \vdash CCGGTTCCGT GGGACCACTG Ы \vdash GGCCAAGGCA U Styl Ø C CCTAATAACC GGATTATTGG 3 GGCGATGGCT TTTATGCGAT AAATACGCTA $\mathbf{\Xi}$ Þ \succ 禸 CCGCTACCGA Ç \Box ტ . .

V S S BlpI ~~~~~~ GGTTAGCTCA G CCAATCGAGT C FIG. 5F

 \vdash GCTGGGTTTG GGAAAGCCCT CGAGTGGCTG GACCTAAGCG GTCGGCGAC CCTTTCGGGA GCTCACCGAC TAGCCTGTCC ACGTCTGGCG TGCAGACCGC CGACCCAAAC 口 \mathcal{O} Ø \geq S \vdash 口 \vdash XhoI Д CTGGTGAAAC GACCACTTTG ATCGGACAGG ഗ 又 Q 口 X ഗ 口 C CCTGACCCTG ACCTGTACCT TTTCCGGATT CAGCCGCCTG ACTITICITIC GCCGGGCCGG TGGACATGGA AAAGGCCTAA 2299222992 H Þ BSPEI Д BstXI ~~~~~ Ċ Д Д S C \circ CAGGTGCAAT TGAAAGAAAG ſщ CTGGATTCGC ഗ 斘 \vdash 口 Н \mathcal{O} X 3 \vdash 22222 O Mfei GTCCACGTTA TTGGCGTGGG GGACTGGGAC AACCGCACCC C 口 H O ᆸ Q >

FIG. 5G

| D W D D K Y Y S T S L K T MluI | TATAGCACCA GCCTGAAAAC ATATCGTGGT CGGACTTTTG | T J V V Z I | AAATCAGGTG GTGCTGACTA TTTAGTCCAC CACGACTGAT | D P V D T A T Y Y C A R W BSSHII | CCTATTATTG CGCGCGTTGG |
|--------------------------------|------------------------------------------------|------------------------|------------------------------------------------|----------------------------------|------------------------------------------------|
| D W D D K Y | ATTGGGATGA TGATAAGTAT TAACCCTACT ACTATTCATA | ISKDTSKNVQVVLT NspV | • – | | GGACCCGGTG GATACGGCCA CCTGGGCCAC CTATGCCGGT |
| A L I | GCTCTGATTG CGAGACTAAC | R L T MluI | GCGTCTGACC CGCAGACTGG | M T M | TGACCAACAT ACTGGTTGTA |

FIG. 5H

| \triangleright | GT | | |
|-------------------------------|------------------------------------------------|-------------------------------------------|--------------------------|
| 디 | CTG | | |
| N I I ∼ | TGGGGCCAAG GCACCCTGGT ACCCCGGTTC CGTGGGACCA | | |
| ρ T Σ | တို့ ပွ | | |
| Q G StyI ~~~~~~~ | CAA | | |
| ტ ' | 390 | | |
| M | TGG(| | |
| ≻⊣ | | | |
| Ω | GAT | | |
| G F Y A M D Y W G Q G Styl | GATGGATTAT TGGGGCCAAG CTACCTAATA ACCCCGGTTC | | |
| A | 19C 10G | | |
| ≻ | TAT | | |
| Įт | GCTTTTATGC CGAAAATACG | ω H .> | TCAG AGTC |
| O | | ე ~~ | |
| Ω . | GGCGGCGATG CCGCCGCTAC | Ω . M . | GACGGTTAGC CTGCCAATCG |
| О | 3000 3000 | Ω ≥El | GGT |
| CD | GGCGGCGATG CCGCCGCTAC | E | GAC |
| | | | |

FIG. 51

| P\ | |
|----|--|
| | |
| _ | |
| • | |
| • | |

S AGCTATGCGA GGTGAGCGCG CGGGCGGCAG GCCGCCCGTC TCGATACGCT CCACTCGCGC Þ K C S O >S Д CTGGTGCAAC ATGGAAATCG CAGAGCTCAC TACCTTTAGC GACCACGTTG GTCTCGAGTG 3 ഗ Q L E XhoI ſщ \vdash 口 C BOOBOOBOOB GGAGGCCTAA CGCGGTTCGG GGACCCTTCC CGGCGGCGGC CCTCCGGATT GCGCCAAGCC CCTGGGAAGG L Ç S BSPEI × Ç C \mathcal{O} Д Þ GAAGTGCAAT TGGTGGAAAG ACCACCTTTC TCGACGCGCC ഗ Þ Þ 口 O \mathcal{O} \gt 召 ഗ Q MfeI CTTCACGTTA GGACGCAGAC TGAGCTGGGT CCTGCGTCTG ACTCGACCCA Ц 3 召 ഗ \Box 口 \boxtimes

FIG. 5J

 α CGCCTATCGC ACTTTCCGGC Ċ GCGGATAGCG ഗ Д T Y Y CACCTATTAT GTGGATAATA S G G S S GCGCCAG TAATCGCCAT CGCCGCCGTC ഗ ATTAGCGGTA ტ ഗ

 \boxtimes 口 Ц E Z ¥ NspVഗ Z Д Pmlr ഗ \mathbf{H} \vdash L

GACGTTTACT ATTCGAAAAA CACCCTGTAT CTGCAAATGA GTGGGACATA TAAGCTTTTT AGTGCACTAT TCACGTGATA AAAATGGTAA TTTACCATT

召 Н BSSHI \succ > EagI Ø Н \Box 口 D 召 Ц S Z

 \mathcal{O}

3

ATTATTGCGC GCGTTGGGGC CGCAACCCCG TAATAACGCG ACGGCCGTGT TGCCGGCACA TGCGGAAGAT ACGCCTTCTA ACAGCCTGCG TGTCGGACGC

FIG. 5K

| \vdash | | AC TG |
|-----------------------------------|---------------|--------------------------|
| \gt | | GTG |
| Y A M D Y W G Q G T L V T Styl | | CCCTGGTGAC GGGACCACTG |
| | | CA TO TI |
| r D | ? | S C C C C |
| Q (Styl | ~ ~ ~ ~ ~ ~ ~ | GGCCAAGGCA CCGGTTCCGT |
| Ü | ′ | 000 |
| M | | TGG |
| \succ | | TAT ATA |
| Ω | | GGATTATTGG CCTAATAACC |
| Σ | | AT: |
| Ø | | 0001 0001 |
| | | TTTATGCGAT AAATACGCTA |
| Įт | | |
| CD | | `GG(\CC(|
| Ω | | GGCGATGGCT CCGCTACCGA |
| O | | 900 |

FIG. 5L

 \vdash GCTCGCTTTG CGAGCGAAAC TCGATAATAA AGCTATTATT \succ 口 \mathcal{O} ഗ Hഗ Д CTGGTGAAAC GACCACTTTG CAGCATTAGC GTCGTAATCG 3 ഗ 又 L E XhoI \mathbf{H} > ഗ ᆸ \mathcal{O} ACCAGGCCCG TTTCCGGAGG AAAGGCCTCC TGGTCCGGGC \mathcal{O} O, S G BspEI 又 ~~~~ Д Ç Ç Д >ACGTTCTTTC TGCAAGAAAG TGGACGTGGC ACCTGCACCG ഗ Д \vdash 口 O \mathcal{O} Ø 召 \vdash Q MfeI GTCCACGTTA CAGGTGCAAT GGACTCGGAC Н Н 3 ഗ ഗ 口 Ø 3

F/G. 5M

TTTGACTCGT GATTGGCTAT AAAGCCGGGT TTTCGGCCCA AAACTGAGCA CTAACCGATA **₹** \mathcal{O} BstEI ഗ α G 口 ഗ 3 又 又 CCGAGCCTGA GTCTCGAGTG CAGAGCTCAC GGCTCGGACT GTTTAGCCTG CAAATCGGAC 召 口 口 BSSHI Þ ഗ ഗ 口 Д GTTGATACTT CGAAAAACCA GCTTTTTGGT ATTTATTATA GCGGCAGCAC CAACTATAAT CCTGGGAAGG GGACCCTTCC GTTGATATTA O Z Z \succ × ~~~~~ \mathbb{Z} NspVEagl D ഗ CAACTATGAA CGCCGTCGTG GGAGCTGGAT TCGCCAGCCG AGCGGTCGGC \vdash Е \vdash S О Ċ Þ > S CCTCGACCTA TAAATAATAT GACCATTAGC CTGGTAATCG ď ഗ \vdash T I BstEII > ~ ~ ~ ~ Н S

FIG. 5N

| GCCGTGTATT ATTGCGCGCG TTGGGGCGGC CGGCACATAA TAACGCGCGC AACCCCGCCG | Y A M D Y W G Q G T L V T V Styl | PACCC TGGTGACGGT FTGGG ACCACTGCCA |
|----------------------------------------------------------------------|----------------------------------|----------------------------------------------------------------------|
| ATTGCG | O G Styl | CAAGGCACCC GTTCCGTGGG |
| GCCGTGTATT CGGCACATAA | D M | ATGCGATGGA TTATTGGGGC CAAGGCACCC TACGCTACCT AATAACCCCG GTTCCGTGGG |
| GGCGGATACG CCGCCTATGC | Z A M D | ATGCGATGGA TACGCTACCT |
| GCGTGACGGC CGCACTGCCG | D G Y | GATGGCTTTT CTACCGAAAA |

FIG. 50

S

CGGCGAAAG GCCGCTTTC TCGATAACCT GATGGGCATT CTACCCGTAA AGCTATTGGA \mathbf{H} 3 口 \mathcal{O} \succ C Σ S Д GTCTCGAGTG GTGAAAAAAC CACTTTTTG CAGAGCTCAC TTCCTTTACG AAGGAAATGC \geq Еч ¥ ~~~~~ L E XhoI ш 又 S >Ċ ACCAAGTCTC GCCGCGCCTT GCGCCAGATG CCTGGGAAGG CGCGGTCTAC GGACCCTTCC CGGCGCGGAA GTTCCGGATA CAAGGCCTAT \succ 口 S BSPEI 又 ~ ~ ~ ~ ~ ~ ~ K O C Д ~~~~~~~~ $^{\circ}$ TGGTTCAGAG TCGACGTTTC AGCTGCAAAG ഗ Ξ X \circ Ø \mathcal{O} > 召 ഗ Q Mfel CTTCACGTTA TTGGCTGGGT AACCGACCCA GAAGTGCAAT GGACTTTTAA CCTGAAAATT >3 \bowtie \mathcal{O} 口 口 H

TAATAACGCG CGCAACCCCG ATTATTGCGC GCGTTGGGGC GAAGTTACCT AGAGGCTCGA AAGTCCCGGT CACCGCGTAT CTTCAATGGA \mathcal{O} 3 3 Ø 召 口 Щ BSSHI GTGGCGCATA Þ TCTCCGAGCT ഗ Q Д × \vdash S \succ AAAGCATTAG GCAGCCTGAA AGCGAGCGAT ACGGCCATGT TTTCGTAATC TGCCGGTACA ATGGGCAATA T R Y TACCCGTTAT S Σ HQ ഗ \vdash × TAAATAGGCC CGCTATCGCT TCGCTCGCTA AGCGCGGATA TCGCGCCTAT \Box GCGATAGCGA \Box \Box ഗ S K Д Z, ഗ Ċ GGTGACCATT CCACTGGTAA CGTCGGACTT 又 \vdash Д Ы ~~~~~ V T BstEII S S

FIG.50

| L V | CCCTGGTGAC GGGACCACTG | |
|-------------------------------------|--------------------------------|-----|
| Styl | GGCCAAGGCA CO | |
| O X Q | GGATTATTGG GC CCTAATAACC CC | |
| F Y A M D Y W G Q G T L V T Styl | TTTATGCGAT G AAATACGCTA C | |
| щ О О | GGCGATGGCT CCGCTACCGA | S S |

-1G.5R

| L Q Q S G P G L V K P S Q T I | | T C A I S G D S V S S N S BSPEI | ACCTGTGCGA TTTCCGGAGA TAGCGTGAGC AGCAACAGCG TGGACACGCT AAAGGCCTCT ATCGCACTCG TCGTTGTCGC | WIRQSPGRGLEWL BstXI Xhoi | GCGTGGC |
|----------------------------------|--------------------------|---------------------------------|--------------------------------------------------------------------------------------------|-----------------------------|--------------------------|
| O V Q L MfeI | CAGGTGCAAT GTCCACGTTA | L S L | CCTGAGCCTG GGACTCGGAC | A A W N | CGGCGTGGAA GCCGCACCTT |
| | | | | | |

FIG. 5S

GTCAAATCGG TTATTGCGCG TTGCTAATAC GCCACTCGCA CAGTTTAGCC CGGTGAGCGT BSSHII ~ ~ ~ ~ ~ ~ S \succ Q K AACGATTATG TTCGAAAAAC AAGCTTTTTG CGGCCGTGTA GCCGCCACAT Z ~ ~ ~ ~ ~ ~ NspVEagI Þ ഗ \vdash TGGGCCTATG CCGGAAGATA ACCCGGATAC GGCCTTCTAT CCGGCATGGA TAATAGCATC GTTTACCATA E П 3 Щ Д Д Z CAGCGTGACC Y R S ATTATCGTAG GTCGCACTGG GAAAAGCCGG ATTACCATCA CTTTTCGGCC TAATGGTAGT \vdash Н BsaBI \gt \vdash ഗ TGCAACTGAA ACGTTGACTT GGCCGTACCT Z 召 口 ß Ø 又 山

FIG. 5T

| \vdash | AC TG | | |
|-----------------------|------------------------------------------------|------------------|--------------------------|
| ආ ⁺ | 000 000 | | |
| DGFYAMDYWGQGT Styl | GCCAAGGCAC CGGTTCCGTG | | |
| Ŋ | | | |
| N | GATTATTGGG CTAATAACCC | | |
| \Rightarrow | TAT | | |
| О | GAI | | |
| Z | ATG TAC | | |
| K. | 909 090 | | |
| × | GCGATGGCTT TTATGCGATG CGCTACCGAA AATACGCTAC | | |
| ĹΉ | TT | , н | AG |
| ტ | 999 | SSBIPI | CTC |
| Д | GCGATGGCTT CGCTACCGAA | V S S Blp | GTTAGCTCAG CAATCGAGTC |
| | 000 | \triangleright | GT C |
| O | | £I | \mathcal{C} |
| O | 0 | | GA |
| R W G G | IGG ACC | L V T | GGT |
| R W BSSHII ~ | CGTTGGGGCG GCAACCCCGC | ᆸ | CCTGGTGACG |

- O1K1 5'- GAATGCATACGCTGATATCCAGATGACCCAGAG-CCCGTCTAGCCTGAGC -3'
- **O1K2** 5'- CGCTCTGCAGGTAATGGTCACACGATCACCCAC-GCTCGCGCTCAGGCTAGACGGC -3'
- **O1K3** 5'- GACCATTACCTGCAGAGCGAGCCAGGGCATTAG-CAGCTATCTGGCGTGGTACCAGCAG ÷3'
- **O1K4** 5'- CTTTGCAAGCTGCTGGCTGCATAAATTAATAGT-TTCGGTGCTTTACCTGGTTCTGCTGGTACCACGCCAG -3'
- **O1K5** 5'- CAGCCAGCAGCTTGCAAAGCGGGGTCCCC-GTTTTAGCGGCTCTGGATCCGGCACTGATTTTAC -3'
- **O1K6** 5'- GATAATAGGTCGCAAAGTCTTCAGGTTGCAGGC-TGCTAATGGTCAGGGTAAAATCAGTGCCGGATCC -3'
- **O2K1** 5'- CGATATCGTGATGACCCAGAGCCCACTGAGCCT-GCCAGTGACTCCGGGCGAGCC -3'
- **O2K2** 5'- GCCGTTGCTATGCAGCAGGCTTTGGCTGCTTCT-GCAGCTAATGCTCGCAGGCTCGCCGGAGTCAC -3'
- **O2K3** 5'- CTGCTGCATAGCAACGGCTATAACTATCTGGAT-TGGTACCTTCAAAAACCAGGTCAAAGCCC -3'
- **O2K4** 5'- CGATCCGGGACCCCACTGGCACGGTTGCTGCCC-AGATAAATTAATAGCTGCGGGCTTTGACCTGGTTTTTG -3'
- **O2K5** 5'- AGTGGGGTCCCGGATCGTTTTAGCGGCTCTGGA-TCCGGCACCGATTTTACCCTGAAAATTAGCCGTGTG -3'
- **O2K6** 5'- CCATGCAATAATACACGCCCACGTCTTCAGCTT-CCACACGCCTAATTTTCAGGG -3'
- O3K1 5'- GAATGCATACGCTGATATCGTGCTGACCCAGAG
- O3K2 5'- CGCTCTGCAGCTCAGGGTCGCACGTTCGCCCGG-AGACAGGCTCAGGGTCGCCGGGCTCTGGGTCAGC -3'
- **O3K3** 5'- CCCTGAGCTGCAGAGCGAGCCAGAGCGTGAGCA-GCAGCTATCTGGCGTGGTACCAG -3'

FIG. 6A

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- GCCATAAATTAATAGACGC
- O3K4 5'- GCACGGCTGCTCGCGCCATAAATTAATAGACGC-GGTGCTTGACCTGGTTTCTGCTGGTACCACGCCAGATAG -3'
- O3K5 5'- GCGCGAGCAGCCGTGCAACTGGGGTCCCGGCGC-GTTTTAGCGGCTCTGGATCCGGCACGGATTTTAC -3'
- **O3K6** 5'- GATAATACACCGCAAAGTCTTCAGGTTCCAGGC-TGCTAATGGTCAGGGTAAAATCCGTGCCGGATC -3'
- **O4K1** 5'- GAATGCATACGCTGATATCGTGATGACCCAGAG-CCCGGATAGCCTGGCG -3'
- **O4K2** 5'- GCTTCTGCAGTTAATGGTCGCACGTTCGCCCAG-GCTCACCGCCAGGCTATCCGGGC -3'
- **O4K3** 5'- CGACCATTAACTGCAGAAGCAGCCAGAGCGTGC-TGTATAGCAGCAACAACAAAACTATCTGGCGTGGTACCAG
- **O4K4** 5'- GATGCCCAATAAATTAATAGTTTCGGCGGCTGA-CCTGGTTCTGCTGGTACCACGCCAGATAG -3'
- **O4K5** 5'- AAACTATTAATTTATTGGGCATCCACCCGTGAA-AGCGGGGTCCCGGATCGTTTTAGCGGCTCTGGATCCGGCAC-3'
- **O4K6** 5'- GATAATACACCGCCACGTCTTCAGCTTGCAGGG-ACGAAATGGTCAGGGTAAAATCAGTGCCGGATCCAGAGCC-3'
- **O1L1** 5'- GAATGCATACGCTCAGAGCGTGCTGACCCAGCC-GCCTTCAGTGAGTGG -3'
- **O1L2** 5'- CAATGTTGCTGCTGCTGCCGCTACACGAGATGG-TCACACGCTGACCTGGTGCGCCACTCACTGAAGGCGGC -3'
- **O1L3** 5'- GGCAGCAGCAGCAACATTGGCAGCAACTATGTG-AGCTGGTACCAGCAGTTGCCCGGGAC -3'
- O1L4 5'- CCGGCACGCCTGAGGGACGCTGGTTGTTATCAT-AAATCAGCAGTTTCGGCGCCGTCCCGGGCAACTGC -3
 O1L5 5'- CCCTCAGGCGTGCCGGATCGTTTTAGCGGATCC-

AAAAGCGGCACCAGCGCGAGCCTTGCG -3'

FIG.6B

Achim KNAPPIK et al. PROTEIN/ (POLY) PEPTIDE LIBRARIES Application No. 09/490,324

- **O1L6** 5'- CCGCTTCGTCTTCGCTTTGCAGGCCCGTAATCG-CAAGGCTCGCGCTGG -3'
- **O2L1** 5'- GAATGCATACGCTCAGAGCGCACTGACCCAGCC-AGCTTCAGTGAGCGGC -3'
- **O2L2** 5'- CGCTGCTAGTACCCGTACACGAGATGGTAATGC-TCTGACCTGGTGAGCCGCTCACTGAAGCTGG -3'
- **O2L3** 5'- GTACGGGTACTAGCAGCGATGTGGGCGGCTATA-ACTATGTGAGCTGGTACCAGCAGCATCCCGG -3'
- **O2L4** 5'- CGCCTGAGGGACGGTTGCTCACATCATAAATCA-TCAGTTTCGGCGCCCTTCCCGGGATGCTGCTGGTAC -3'
- **O2L5** 5'- CAACCGTCCCTCAGGCGTGAGCAACCGTTTTAG-CGGATCCAAAAGCGGCAACACCGCGAGCC -3'
- **O2L6** 5'- CCGCTTCGTCTTCCGCTTGCAGGCCGCTAATGG-TCAGGCTCGCGGTGTTGCCG -3'
- **O3L1** 5'- GAATGCATACGCTAGCTATGAACTGACCCAGCC-GCCTTCAGTGAGCG -3'
- **O3L2** 5'- CGCCCAGCGCATCGCCGCTACACGAGATACGCG-CGTCTGACCTGGTGCAACGCTCACTGAAGGCGGC -3'
- **O3L3** 5'- GGCGATGCGCTGGGCGATAAATACGCGAGCTGG-TACCAGCAGAAACCCGGGCAGGCGC -3'
- **O3L4** 5'- GCGTTCCGGGATGCCTGAGGGACGGTCAGAATC-ATCATAAATCACCAGAACTGGCGCCTGCCCGGGTTTC -3'
- **O3L5** 5'- CAGGCATCCCGGAACGCTTTAGCGGATCCAACA-GCGCCAACACCGCGACCCTGACCATTAGCGG -3'
- **O3L6** 5'- CCGCTTCGTCTTCCGCCTGAGTGCCGCTAATGG-TCAGGGTC -3'
- O1246H1 5'- GCTCTTCACCCCTGTTACCAAAGCCCAG-GTGCAATTG -3'
- **O1AH2**5'- GGCTTTGCAGCTCACTTTCACGCTGCTGCCCGGT-TTTTCACTTCCGCGCCAGACTGAACCAATTGCACCTGGGC-TTTG -3'

FIG. 6C

- **O1AH3** 5'- GAAAGTGAGCTGCAAAGCCTCCGGAGGCACTTT-TAGCAGCTATGCGATTAGCTGGGTGCGCCAAGCCCCTGGGCAGGCTC -3'
- **O1AH4** 5'- GCCCTGAAACTTCTGCGCGTAGTTCGCCGTGCCA-AAAATCGGAATAATGCCGCCCATCCACTCGAGACCCTGCCC-AGGGGC -3'
- **O1AH5** 5'- GCGCAGAAGTTTCAGGGCCGGGTGACCATTACC-GCGGATGAAAGCACCAGCACCGCGTATATGGAACTGAGCAGCCTGCG -3'
- **O1ABH6** 5'- GCGCGCAATAATACACGGCCGTATCTTCGCT-ACGCAGGCTGCTCAGTTCC -3'
- **O1BH2** 5 '- GGCTTTGCAGCTCACTTTCACGCTCGCGCCCGGT-TTTTCACTTCCGCGCCGCCTCTGAACCAATTGCACCTGGGC-TTTG -3 '
- **O1BH4** 5'- GCCCTGAAACTTCTGCGCGTAGTTCGTGCCGCC-GCTATTCGGGTTAATCCAGCCCATCCACTCGAGACCCTGCCCAGGGGC -3'
- **O1BH5** 5'- GCGCAGAAGTTTCAGGGCCGGGTGACCATGACC-CGTGATACCAGCATTAGCACCGCGTATATGGAACTGAGCAGCCTGCG -3'
- **O2H3** 5'- CTGACCCTGACCTGTACCTTTTCCGGATTTAGC-CTGTCCACGTCTGGCGTTGGCGTGGGCTGGATTCGCCAGCCGCCTGGGAAAG -3
- **O2H4** 5'- GCGTTTTCAGGCTGGTGCTATAATACTTATCAT-CATCCCAATCAATCAGAGCCAGCCACTCGAGGGCTTTCCCAGGCGCTGG -3'

FIG. 6D

Achim KNAPPIK et al. PROTEIN/ (POLY) PEPTIDE LIBRARIES Application No. 09/490,324

- **O2H5** 5'- GCACCAGCCTGAAAACGCGTCTGACCATTAGCA-AAGATACTTCGAAAAATCAGGTGGTGCTGACTATGACCAACAT GG -3'
- **O2H6** 5'- GCGCGCAATAATAGGTGGCCGTATCCACCGGGT-CCATGTTGGTCATAGTCAGC -3'
- **O3H1** 5'- CGAAGTGCAATTGGTGGAAAGCGGCGGCCT-GGTGCAACCGGGCGGCAG -3'
- O3H2 5'- CATAGCTGCTAAAGGTAAATCCGGAGGCCGCC-AGCTCAGACGCAGGCTGCCGCCCGGTTGCAC -3'
- O3H3 5'- GATTTACCTTTAGCAGCTATGCGATGAGCTGGG-TGCGCCAAGCCCCTGGGAAGGGTCTCGAGTGGGTGAG -3'
- O3H4 5'- GGCCTTTCACGCTATCCGCATAATAGGTGCTGC-CGCCGCTACCGCTAATCGCGCTCACCCACTCGAGACCC -3'
- **O3H5** 5'- CGGATAGCGTGAAAGGCCGTTTTACCATTTCAC-GTGATAATTCGAAAAAACACCCTGTATCTGCAAATGAACAG-3'
- **O3H6** 5'- CACGCGCGCAATAATACACGGCCGTATCTTCCG-CACGCAGGCTGTTCATTTGCAGATACAGG -3'
- **O4H2** 5'- GGTCAGGCTCAGGGTTTCGCTCGGTTTCACCAG-GCCCGGACCACTTTCTTGCAATTGCACCTGGGCTTTG -3'
- **O4H3** 5'- GAAACCCTGAGCCTGACCTGCACCGTTTCCGGAGG-CAGCATTAGCAGCTATTATTGGAGCTGGATTCGCCAGCCGC-3'
- **O4H4** 5'- GATTATAGTTGGTGCTGCCGCTATAATAAATAT-AGCCAATCCACTCGAGACCCTTCCCAGGCGGCTGGCGAATCCAGG-3'
- **O4H5** 5'- CGGCAGCACCAACTATAATCCGAGCCTGAAAAG-CCGGGTGACCATTAGCGTTGATACTTCGAAAAACCAGTTTAGCCTG -3'
- **O4H6** 5'- GCGCGCAATAATACACGGCCGTATCCGCCGCCG-TCACGCTGCTCAGTTTCAGGCTAAACTGGTTTTTCG -3'

FIG. 6E

Achim KNAPPIK et al. PROTEIN/ (POLY) PEPTIDE LIBRARIES Application No. 09/490,324

- **O5H1** 5'- GCTCTTCACCCCTGTTACCAAAGCCGAAGTGCA ATTG -3'
- **O5H2** 5'- CCTTTGCAGCTAATTTTCAGGCTTTCGCCCGGT-TTTTTCACTTCCGCGCCGCTCTGAACCAATTGCACTTCGGCTTTGG -3'
- **O5H4** 5'- CGGAGAATAACGGGTATCGCTATCGCCCGGATA-AATAATGCCCATCCACTCGAGACCCTTCCCAGGCATCTGGCGCAC -3'
- **O5H5** 5'- CGATACCCGTTATTCTCCGAGCTTTCAGGGCCA-GGTGACCATTAGCGCGGATAAAAGCATTAGCACCGCGTATCTTC-3'
- **O5H6** 5'- GCGCGCAATAATACATGGCCGTATCGCTCGCTT-TCAGGCTGCTCCATTGAAGATACGCGGTGCTAATG -3'
- **O6H2** 5'- GAAATCGCACAGGTCAGGCTCAGGGTTTGGCTC-GGTTTCACCAGGCCCGGACCAGACTGTTGCAATTGCACCTGG-GCTTTG -3'
- **O6H3** 5 ' GCCTGACCTGTGCGATTTCCGGAGATAGCGTGA-GCAGCAACAGCGCGGCGTGGAACTGGATTCGCCAGTCTCCTGGGCG-3 '
- **O6H4** 5'- CACCGCATAATCGTTATACCATTTGCTACGATA-ATAGGTACGGCCCAGCCACTCGAGGCCACGCCCAGGAGACTGGCG-3'
- **O6H5** 5'- GGTATAACGATTATGCGGTGAGCGTGAAAAGCC-GGATTACCATCAACCCGGATACTTCGAAAAACCAGTTTAGCCTGC -3'
- **O6H6** 5'- GCGCGCAATAATACACGGCCGTATCTTCCGGGG-TCACGCTGTTCAGTTGCAGGCTAAACTGGTTTTTC-3'
- **OCLK1** 5'- GGCTGAAGACGTGGGCGTGTATTATTGCCAGCA-GCATTATACCACCCGCCGACCTTTGGCCAGGGTAC -3'

FIG. 6F

- **OCLK2** 5'- GCGAAAAATAAACACGCTCGGAGCAGCCACCG-TACGTTTAATTTCAACTTTCGTACCCTGGCCAAAGGTC -3'
- OCLK3 5'- GAGCGTGTTTATTTTTCCGCCGAGCGATGAACA-ACTGAAAAGCGGCACGGCGAGCGTGTGCCTGCTG -3'
- **OCLK4** 5'- CAGCGCGTTGTCTACTTTCCACTGAACTTTCGC-TTCACGCGGATAAAAGTTGTTCAGCAGGCACACCACGC -3'
- **OCLK5** 5'- GAAAGTAGACAACGCGCTGCAAAGCGGCAACAG-CCAGGAAAGCGTGACCGAACAGGATAGCAAAGATAG -3'
- **OCLK6** 5'- GTTTTTCATAATCCGCTTTGCTCAGGGTCAGGG-TGCTGCTCAGAGAATAGGTGCTATCTTTGCTATCCTGTTCG -3'
- **OCLK7** 5'- GCAAAGCGGATTATGAAAAACATAAAGTGTATG-CGTGCGAAGTGACCCATCAAGGTCTGAGCAGCCCGGTG -3'
- **OCLK8** 5'- GGCATGCTTATCAGGCCTCGCCACGATTAAAAG-ATTTAGTCACCGGGCTGCTCAGAC -3'
- **OCH1** 5'- GGCGTCTAGAGGCCAAGGCACCCTGGTGACGT-TAGCTCAGCGTCGAC -3'
- OCH2 5'- GTGCTTTTGCTGCTCGGAGCCAGCGGAAACACG-CTTGGACCTTTGGTCGACGCTGAGCTAACC -3'
- OCH3 5'- CTCCGAGCAGCAAAAGCACCAGCGGCGCACGG-CTGCCCTGGGCTGCCTGGTTAAAGATTATTTCC -3'
- **OCH4** 5'- CTGGTCAGCGCCCCGCTGTTCCAGCTCACGGTG-ACTGGTTCCGGGAAATAATCTTTAACCAGGCA -3'
- **OCH5** 5'- AGCGGGGCGCTGACCAGCGGCGTGCATACCTTT-CCGGCGGTGCTGCAAAGCAGCGGCCTG -3'
- **OCH6** 5'- GTGCCTAAGCTGCTCGGCACGGTCACAACG-CTGCTCAGGCTATACAGGCCGCTGCTTTGCAG -3'
- **OCH7** 5'- GAGCAGCAGCTTAGGCACCTATATTTG-CAACGTGAACCATAAACCGAGCAACACC -3'
- **OCH8** 5'- GCGCGAATTCGCTTTTCGGTTCCACTTTTTTAT-CCACTTTGGTGTTGCTCGGTTTATGG -3'

FIG. 6G

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AAAGGCGGCT CGCTACTTGT TTTCCGCCGA GCGATGAACA CGTACGGTGG CTGCTCCGAG CGTGTTTATT GACGAGGCTC GCACAAATAA GCATGCCACC

CCGTGCCGCT CGCACCACAC GGACGACTTG TTGAAATAG AACTTTTATC GGCACGGCGA GCGTGGTGTG CCTGCTGAAC L L ഗ T ტ L K S ACTGAAAAGC TGACTTTTCG

P R E A K V Q W K V D N A L Q S G CGCGTGAAGC GAAAGTTCAG TGGAAAGTAG ACAACGCGCGT GCAAAGCGGC GCGCACTICG CTITCAAGIC ACCITICAIC IGITGCGCGA CGITICGCCG

AACAGCCAGG AAAGCGTGAC CGAACAGGAT AGCAAAGATA GCACCTATTC TIGICGGICC ITICGCACIG GCTIGICCIA ICGITICIAI CGIGGATAAG ഗ M D D O E ഗ 口 о 2

FIG. 7A

GGATTATGAA AAACATAAAG ACTCGTTTCG CCTAATACTT TTTGTATTTC 又 口 TGAGCAAAGC AGACTCGTCG TGGGACTGGG L S S T L T L TCTGAGCAGC ACCCTGACCC

GTAGTTCCAG ACTCGTCGGG CCACTGATTT Д ഗ ഗ CATCAAGGTC ACATACGCAC GCTTCACTGG 闰 \gt

口 C 召 Z Гщ ഗ SphI StuI

GIGGCGAGGC CIGATAAGCA IGC CACCGCTCCG GACTATTCGT ACG AGAAAATTAG TCTTTTAATC

FIG. 7B

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AAGGCGACCG AGGCTCGTCG GCTCAGCGTC GACCAAAGGT CCAAGCGTGT TTCCGCTGGC TCCGAGCAGC GGTTCGCACA CGAGTCGCAG CTGGTTTCCA

G C L V K D Y GGCTGCCTGG TTAAAGATTA CCGACGGACC AATTTCTAAT TTTTCGTGGT CGCCGCCGTG CCGACGGGAC K S T S G G T A A L AAAAGCACCA GCGCGGCAC GGCTGCCTG

CCAGTCACCG TGAGCTGGAA CAGCGGGGCG CTGACCAGCG GGTCAGTGGC ACTCGACCTT GTCGCCCCGC GACTGGTCGC Ċ ഗ N M TTTCCCGGAA AAAGGGCCTT

GTGCTGCAAA GCAGCGGCCT GTATAGCCTG CACGACGTTT CGTCGCCGGA CATATCGGAC S G L ഗ CTTTCCGGCG GAAAGGCCGC GCGTGCATAC CGCACGTATG

FIG. 7C

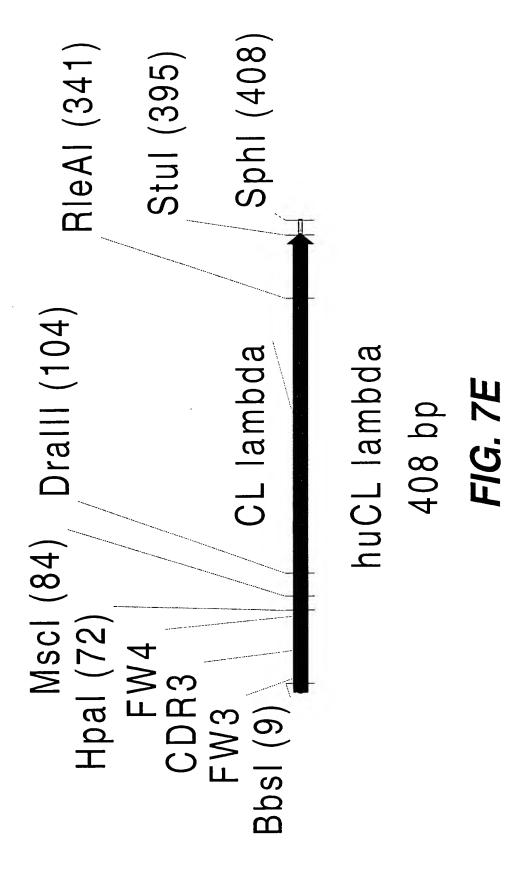
AATCCGTGAG TCTGGATATA Ø \vdash Ċ S S S GAGCAGCAGC AGCAGCGTTG TGACCGTGCC TCGTCGCAAC ACTGGCACGG

ഗ Д AACGTTGCAC Z

EcoRI HindI

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AACCGAAAAG CGAATTCTGA TAAGCTT TTGGCTTTTC GCTTAAGACT ATTCGAA FIG. 7D



|              | 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 |                          |                                                                      |                          |                          |
|--------------|-----------------------------------------|--------------------------|----------------------------------------------------------------------|--------------------------|--------------------------|
| $\leftarrow$ | GAAGACGAAG<br>CTTCTGCTTC                | CGGATTATTA<br>GCCTAATAAT | CGGATTATTA TTGCCAGCAG CATTATACCA<br>GCCTAATAAT AACGGTCGTC GTAATATGGT | CATTATACCA<br>GTAATATGGT | CCCCGCCTGT<br>GGGGCGGACA |
|              |                                         | dH<br>·~~                | HpaI<br>~~~~~~                                                       | MscI                     | DraIII                   |
| 51           | GTTTGGCGGC                              | GGCACGAAGT TAACCGTTCT    | TAACCGTTCT                                                           | TGGCCAGCCG               | AAAGCCGCAC               |
|              | CAAACCGCCG                              | CCGTGCTTCA               | CCGTGCTTCA ATTGGCAAGA                                                | ACCGGTCGGC               | 'I"I'I'CGGCG'I'G         |
|              | DraIII                                  |                          |                                                                      |                          |                          |
|              | <pre></pre>                             |                          |                                                                      |                          |                          |
| 101          | CGAGTGTGAC                              | GCTGTTTCCG               | GCTGTTTCCG CCGAGCAGCG AAGAATTGCA GGCGAACAAA                          | AAGAATTGCA               | GGCGAACAAA               |
|              | GCTCACACTG                              | CGACAAAGGC               | GGCTCGTCGC                                                           | TTCTTAACGT               | CCGCTTGTTT               |
| 151          | GCGACCCTGG                              | TGTGCCTGAT               | TGTGCCTGAT TAGCGACTTT                                                | TATCCGGGAG               | CCGTGACAGT               |
|              | CGCTGGGACC                              | ACACGGACTA               | ACACGGACTA ATCGCTGAAA ATAGGCCCTC                                     |                          | GGCACTGTCA               |

BbsI

# FIG. 7F

| . 201 GGCCTGGAAG GCA<br>CCGGACCTTC CGT                                                     | 251 CACCCTCCAA ACA<br>GTGGGAGGTT TGT                                                       | 301 CTGACGCCTG AGC<br>GACTGCGGAC TCG                                                                          |
|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| GCAGATAGCA<br>CGTCTATCGT                                                                   | AAAGCAAC<br>TTTCGTTG                                                                       | AGCAGTGGAA<br>TCGTCACCTT                                                                                      |
| GCCCCGTCAA<br>CGGGGCAGTT                                                                   | AACAAGTACG<br>TTGTTCATGC                                                                   | Rleai<br>~~~~~<br>GTCCCACAGA<br>CAGGGTGTCT                                                                    |
| GCAGATAGCA GCCCCGTCAA GGCGGGAGTG GAGACCACCA<br>CGTCTATCGT CGGGGCAGTT CCGCCCTCAC CTCTGGTGGT | ACAAAGCAAC AACAAGTACG CGGCCAGCAG CTATCTGAGC<br>TGTTTCGTTG TTGTTCATGC GCCGGTCGTC GATAGACTCG | RleaI<br>~~~~~~<br>AGCAGTGGAA GTCCCACAGA AGCTACAGCT GCCAGGTCAC<br>TCGTCACCTT CAGGGTGTCT TCGATGTCGA CGGTCCAGTG |
| GAGACCACCA<br>CTCTGGTGGT                                                                   | CTATCTGAGC<br>GATAGACTCG                                                                   | GCCAGGTCAC                                                                                                    |

FIG. 7G

GCATGAGGGG AGCACCGTGG AAAAAACCGT TGCGCCGACT GAGGCCTGAT CGTACTCCCC TCGTGGCACC TTTTTTGGCA ACGCGGCTGA CTCCGGACTA 351

SphI

401 AAGCATGC TTCGTACG FIG. 7H

# M24: assembly PCR

M24-A:

GAAGACAAGCGGATTATTGCCAGCAGCATTATACCACCCCGCCTGTGTTTGGCGGCG-GCACGAAGTTAACCGTTC

M24-B:

CAATTCTTCGCTGCTCGGCGGAAACAGCGTCACACTCGGTGCGGCTTTCGGCTGGCCAA-GAACGGTTAACTTCGTGCCGC

M24-C:

CGCCGAGCAGCGAAGAATTGCAGGCGAACAAAGCGACCCTGGTGTGCCTGATTAGCGACT-TTTATCCGGGAGCCGTGACA

FIG. 71



### M24-D:

TGTTTGGAGGGTGTGGTCTCCACTCCCGCCTTGACGGGGCTGCTATCTGCCTTCCAG-GCCACTGTCACGGCTCCCGG

### M24-E:

CCACACCCTCCAAACAAGCAACAAGTACGCGGCCAGCAGCTATCTGAGCCTGACGC-CTGAGCAGTGGAAGTCCCACAGAAGCTACAGCTG

### M24-F:

GCATGCTTATCAGGCCTCAGTCGGCGCAACGGTTTTTTCCACGGTGCTCCCCTCATGCGT-GACCTGGCAGCTGTAGCTTC

### FIG. 7J

Д  $\vdash$ ш SapI ᆸ Ц Д  $\Box$ П Z, 口 Ø Н Н S Ø X  $\Xi$ 

AATGGCAACG AGAAGTGGGG TTACCGTTGC TCTTCACCCC TGACCGTGAG ATGAAACAAA GCACTATTGC ACTGGCACTC CGTGATAACG TACTTTGTTT

 $\mathcal{O}$ ഗ 口  $\gt$ Q L MfeI  $\gt$ 口 ×  $\succ$ П Ø 幺  $\vdash$ 

 $\gt$ 

GAAAGCGGCG CTTTCGCCGC GCAATTGGTG CGTTAACCAC TTCTACTTCA AAGATGAAGT GCCGACTACA CGGCTGATGT TGTTACCAAA ACAATGGTTT

BSPEI S Ø Ø  $\mathcal{O}$ S 口 召 Ы S C G Д Ø  $\gt$  $\vdash$ O G

CCGTCGGACG CAGACTCGAC GCGCCGGAGG GGCAGCCTGC GTCTGAGCTG CGCGGCCTCC GCGGCCTGGT GCAACCGGGC CGCCGGACCA CGTTGGCCCG

G Д BstXI Ø Ø  $\alpha$ >3 ഗ  $\sum$ K S ഗ ſτι  $\vdash$ BspEI G

GGATTTACCT TTAGCAGCTA TGCGATGAGC TGGGTGCGCC AAGCCCCTGG

CCTAAATGGA AATCGTCGAT ACGCTACTCG ACCCACGCGG TTCGGGGACC

# FIG. 8A

 $\vdash$ ഗ G G ഗ Ċ ഗ Н Ø ഗ  $\gt$ Z XhoI 口 口 ტ X

CCGTCGTGGA GCGCGATTAG CGGTAGCGGC GGCAGCACCT CGCGCTAATC GCCATCGCCG GAAGGGTCTC GAGTGGGTGA CTTCCCAGAG CTCACCCACT

NspV Ŋ Z Д PmlI 召 ഗ H $\vdash$ ഥ 召 G X > ഗ K ×  $\succ$ 

CCATTTCACG TGATAATTCG GGTAAAGTGC ACTATTAAGC ATTATGCGGA TAGCGTGAAA GGCCGTTTTA CCGGCAAAAT ATCGCACTTT TAATACGCCT

EagI  $\Box$ 口 Ø 召  $\Box$ S  $\mathbb{Z}$  $\Xi$ O 口  $\succ$ 니  $\vdash$ Z NspV

TTCTATGCCG CTGCGTGCGG AAGATACGGC GACGCACGCC TTACTTGTCG TGTATCTGCA AATGAACAGC ACATAGACGT TTTTTGTGGG AAAAACACCC

 $\Sigma$ Ø >ſτι C  $\Box$  $\Omega$ G 3 召 Ø EagI

BSSHI

TGCGCGCGTT GGGGCGGCGA TGGCTTTTAT GCGATGGATT

| GCACATAATAACGCGCGCAA CCCCGCCGCT ACCGAAATA CGCTACCTAA Y W G Q G T L V T V S S A G G S Styl Styl | ATTGGGGCCA AGGCACCCTG GTGACGGTTA GCTCAGCGGG TGGCGGTTCT<br>TAACCCCGGT TCCGTGGGAC CACTGCCAAT CGAGTCGCCC ACCGCCAAGA | G G G G G G G G G G G D I ECORV | GGCGGCGGTG GGAGCGGTGG CGGTGGTTCT GGCGGTGGTG GTTCCGATAT<br>CCGCCGCCAC CCTCGCCACC GCCACCAAGA CCGCCACCAC CAAGGCTATA | MTQSPLSLPVTPGEPV BanII | ATGACC CAGAGCCCAC TGAGCCTGCC AGTGACTCCG GGCGAGCCTG<br>TACTGG GTCTCGGGTG ACTCGGACGG TCACTGAGGC CCGCTCGGAC |
|------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------|----------------------------------------------------------------------------------------------------------|
| GCACATAAT<br>Y W G<br>S                                                                        | ATTGGGGCC<br>TAACCCCGG                                                                                           | <u>ი</u>                        | GGCGGCGGT                                                                                                        | V M T<br>ECORV         | CGTGATGACC<br>GCACTACTGG                                                                                 |
| •                                                                                              |                                                                                                                  |                                 |                                                                                                                  |                        |                                                                                                          |

CTGCAGAAGC AGCCAAAGCC TGCTGCATAG CAACGGCTAT GACGTCTTCG TCGGTTTCGG ACGACGTATC GTTGCCGATA

GACGTCTTCG

CGAGCATTAG GCTCGTAATC

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|           | L<br>seI                                             | ~~~<br>ATT<br>TAA                                                                      | Ŋ                                       | 909<br>080                                                                                                       | A                          | GCT                                                                                                              |
|-----------|------------------------------------------------------|----------------------------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|----------------------------|------------------------------------------------------------------------------------------------------------------|
|           | L<br>A                                               | GCT<br>CGA                                                                             | ĹΤι                                     | TTA<br>AAT                                                                                                       | H                          | GAA                                                                                                              |
|           | N Y L D W Y L Q K P G Q S P Q L L<br>KpnI SexAI AseI | ATTGGTACCT TCAAAACCA GGTCAAAGCC CGCAGCTATT TAACCATGGA AGTTTTTGGT CCAGTTTCGG GCGTCGATAA | I Y L G S N R A S G V P D R F S<br>Asel | AATTTATCTG GGCAGCAACC GTGCCAGTGG GGTCCCGGAT CGTTTTAGCG<br>TTAAATAGAC CCGTCGTTGG CACGGTCACC CCAGGGCCTA GCAAAATCGC | GSGSGTDFTLKISRVEA<br>Bamhi | GCTCTGGATC CGGCACCGAT TTTACCCTGA AAATTAGCCG TGTGGAAGCT<br>CGAGACCTAG GCCGTGGCTA AAATGGGACT TTTAATCGGC ACACCTTCGA |
|           | വ                                                    | )<br>(GG                                                                               | О                                       | BAT<br>TA                                                                                                        | 民                          | 300<br>300<br>300                                                                                                |
|           | W                                                    | AAG                                                                                    | Д.,                                     | ~<br>3000<br>3000                                                                                                | ω                          | AGC                                                                                                              |
|           | Ø                                                    | TCA                                                                                    | V<br>.091                               | TCC                                                                                                              | Н                          | באדי                                                                                                             |
|           | G<br>AI                                              | TCAAAAACCA GGTCAAAGCC<br>AGTTTTTGGT CCAGTTTCGG                                         | G V P<br>EcoO1091                       | G GGTCCC                                                                                                         | ×                          | AA 1                                                                                                             |
|           | ъ<br>Sex                                             | CCA                                                                                    | E C                                     | TGG                                                                                                              | H                          | TGA                                                                                                              |
|           | X                                                    | _<br>AAA<br>TTT                                                                        | Οĵ                                      | CAG<br>GTC                                                                                                       | E                          | 000                                                                                                              |
|           | O)                                                   | CAA<br>GTT                                                                             | A                                       | TGC<br>ACG                                                                                                       | Ĺتبا                       | TTA<br>AAT                                                                                                       |
|           |                                                      | T A                                                                                    | 民                                       | <u>ი</u> ი                                                                                                       |                            | T<br>A<br>A                                                                                                      |
|           | l H c                                                | ACC<br>IGG                                                                             | Z                                       | AAC<br>I'TG                                                                                                      | Д                          | CGA                                                                                                              |
|           | K<br>Kp                                              | GGTACC                                                                                 | Ø                                       | AGC.                                                                                                             | H                          | CAC                                                                                                              |
|           | M                                                    | AACTATCTGG ATTGGTACCT<br>TTGATAGACC TAACCATGGA                                         | O                                       |                                                                                                                  | ڻ<br>§                     | 0000<br>0000                                                                                                     |
|           | Ω                                                    | 0<br>0<br>0<br>0                                                                       | ъ                                       | TG                                                                                                               | G S<br>BamHI               | ATC<br>PAG                                                                                                       |
|           | 니                                                    | TCT                                                                                    | ≯₁                                      | ATC                                                                                                              | დ<br>წ Ba                  | GGA                                                                                                              |
|           | ×                                                    | AACTATCTGG<br>TTGATAGACC                                                               | e H                                     | TTT<br>'AAA                                                                                                      | S                          | TCT                                                                                                              |
| <b>',</b> | Z                                                    | AA<br>TT                                                                               | AS                                      | AAT<br>TTA                                                                                                       | Ö                          | 99                                                                                                               |
|           |                                                      |                                                                                        |                                         |                                                                                                                  |                            |                                                                                                                  |

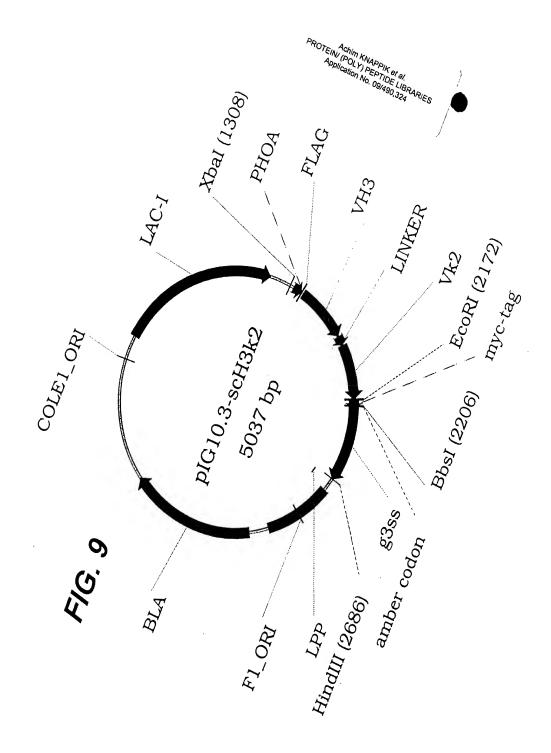
FIG. 8D

CATTATACCA CCCCGCCGAC GTAATATGGT GGGGCGGCTG

GAAGACGTGG GCGTGTATTA TTGCCAGCAG CTTCTGCACC CGCACATAAT AACGGTCGTC

| ۲v.                       | ECORI     | <b>?</b>                                | TTC        | AAG                   |
|---------------------------|-----------|-----------------------------------------|------------|-----------------------|
| Ţ                         | ECC       | ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ | ACGTACGGAA | CTT                   |
| 臼                         | BsiWI     | ;<br>;                                  | \CG(       | PGC(                  |
| $\vdash$                  | BS        | <b>?</b>                                | GTZ        | 3CA.                  |
| 民                         |           | ,                                       |            | L L                   |
| F G Q G T K V E I K R T E |           |                                         | TTGAAATTAA | AACTTTAATT TGCATGCCTT |
| Н                         |           | •                                       | 3AA2       | CTT                   |
| 口                         |           |                                         | TT         | AA(                   |
| >                         |           |                                         | GGTACGAAAG | CCATGCTTTC            |
| 又                         |           |                                         | ACG2       | 555                   |
| ⊣                         |           |                                         | 3GT2       | CAI                   |
| Ċ                         |           |                                         |            |                       |
| Ø                         | MscI      | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \   | CTTTGGCCAG | GAAACCGGTC            |
| <u>ග</u>                  | $\succeq$ | ?                                       | TTG        | AAC                   |
| Щ                         |           |                                         | CJ         | GA                    |

# FIG. 8E

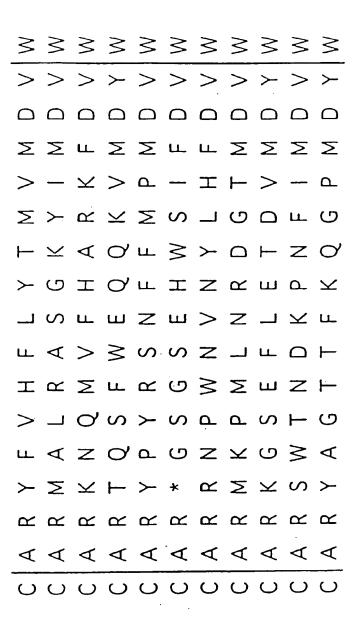


| 103        | >                 | >            | >         | >         | ≯         | ≷         | >         | >         | >         | >         | ≥        | >  | <u>&gt;</u> |
|------------|-------------------|--------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|----|-------------|
| 105        | , <del>&gt;</del> | >            | >         | >         | >         | >         | >-        | >         | >         | >-        | >-       | >  | >-          |
| 101        |                   |              |           |           |           |           |           |           |           |           |          |    |             |
| 300 l      | Σ                 | 1            | •         | ı         | ı         | ı         | ı         | 1         | 1         | ı         | 1        | t  | 1           |
| 100D       | ı                 | ŧ            | ı         | t         | 1         | 1         |           | ı         | 1         | 1         | ı        | ı  | 1           |
| J00 L      | 1                 | 1            | 1         | ı         | ı         | •         | t         | ı         | •         | ı         | ı        | ı  | t           |
| 100B       | $\triangleleft$   | 1            | ı         | •         |           | ı         | •         | •         |           | 1         | •        | ı  | 1           |
| A001       | >-                | •            | 1         | 1         | •         | 1         | t         | ı         | •         | 1         | 1        | ı  | ï           |
| 001        | u.                | >-           | I         | I         | $\propto$ | >-        | ٥         | •         | S         | $\times$  | 4        |    | Σ           |
| 66         | 9                 | Z            | ≷         | >-        | ⋖         | G         | 0         | $\propto$ | Z         | S         | Ø        | >- | ≥           |
| 86         |                   | Σ            | ш         |           | $\prec$   | H         | ⋖         | $\vdash$  | $\propto$ |           | ட        | 0  | ш           |
| <i>46</i>  | Ŋ                 | $\checkmark$ | $\vdash$  | ш         |           | <u>-</u>  | ш         | _         | Z         | ပ         | $\vdash$ | ۵. | S           |
| 96         | 9                 | 9            | $\propto$ | $\propto$ | ய         | Z         | Z         | ⋖         | >-        | >         | $\times$ | 4  | 0           |
| <i>S6</i>  | ≷                 | u.           | エ         | >         | $\times$  | ≥         | _         | <b> </b>  | ≥         | S         | S        | >  | Σ           |
| <i>t</i> 6 | <u>~</u>          | $\propto$    | ∝         | $\propto$ | œ        | ∝  | ~           |
| 83         | ⋖                 | ⋖            | A         | 4         | Ø         | Ø         | ⋖         | 4         | ⋖         | ⋖         | 4        | 4  | ⋖           |
| <i>7</i> 6 | $\overline{o}$    | ပ            | ပ         | C         | ပ         | ပ         | C         | ပ         | ပ         | C         | ပ        | ပ  | O           |
|            |                   |              |           |           |           |           |           |           |           |           |          |    |             |

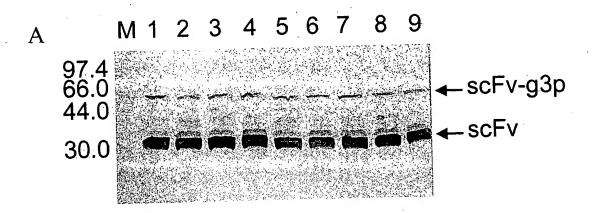
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## FIG. 10A



## FIG. 10B



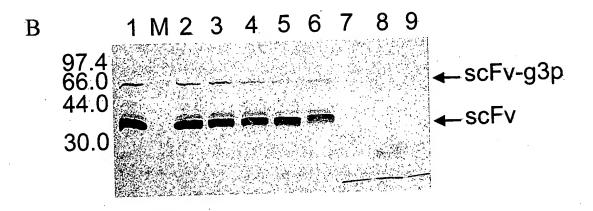


FIG. 11

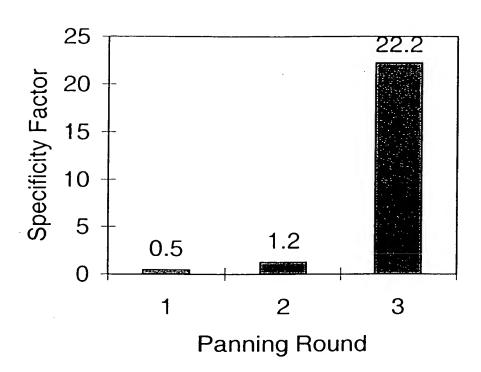


FIG. 12

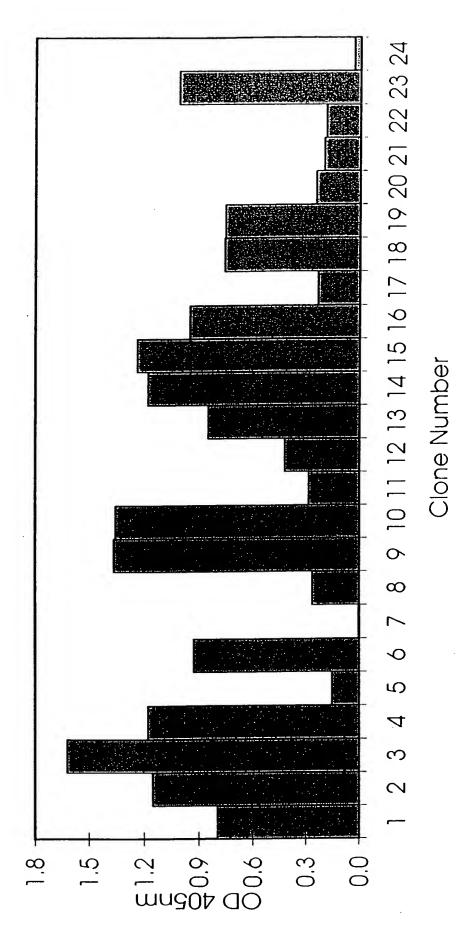
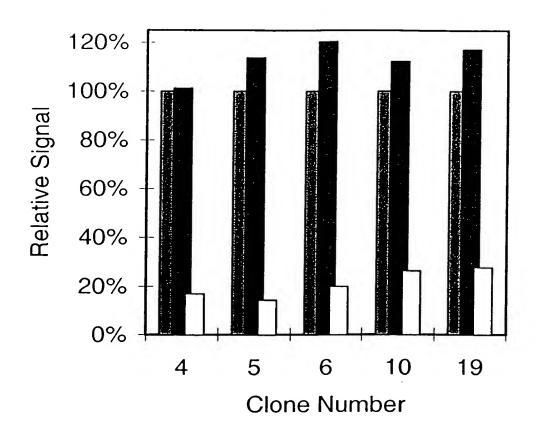
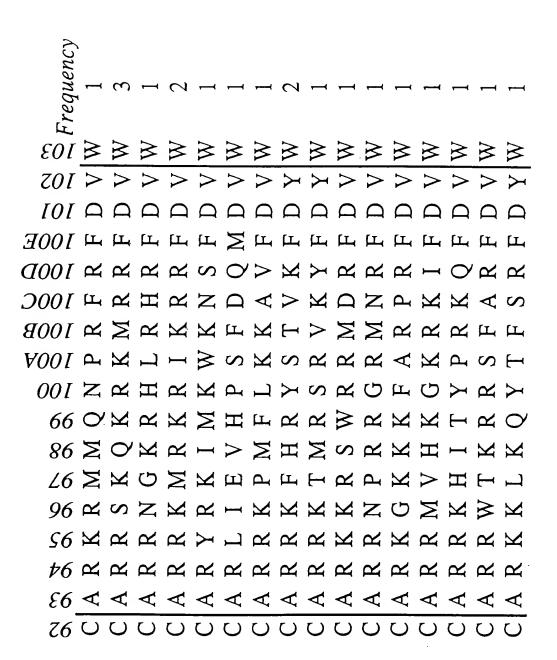


FIG. 13



- No Inhibition
- Inhibition with BSA
- ☐ Inhibition with Fluorescein

FIG. 14



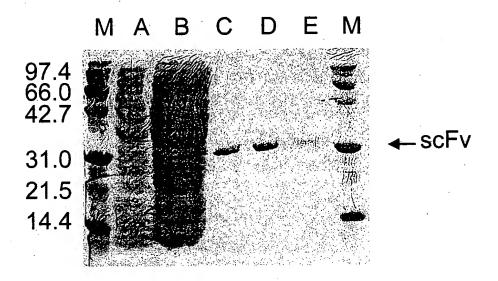
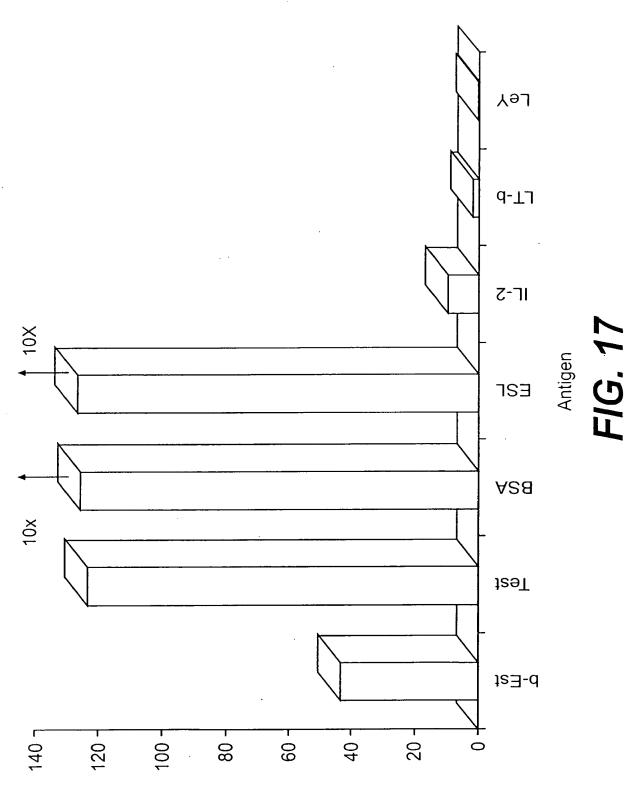
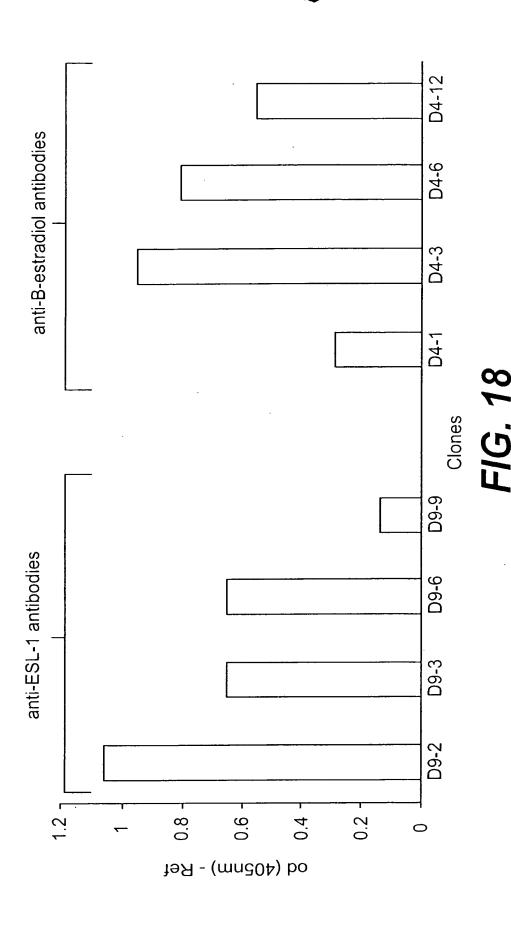
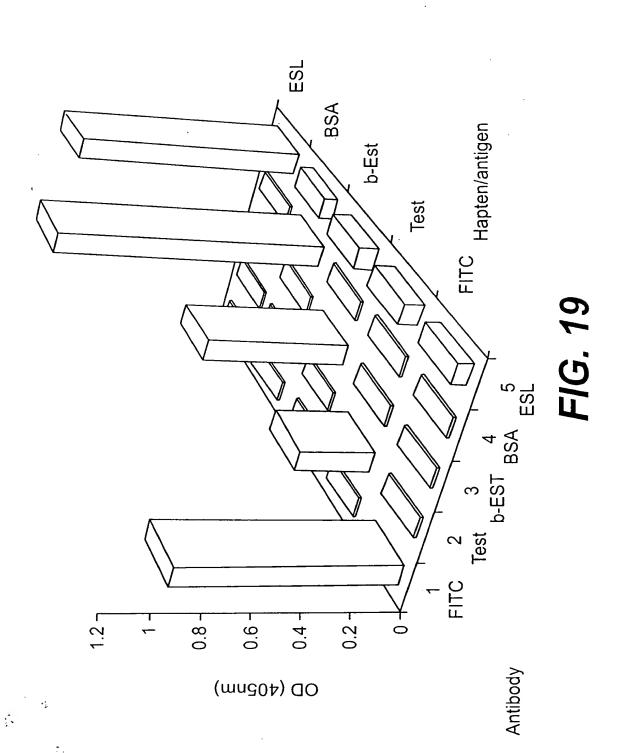


FIG. 16



Enrichment factor





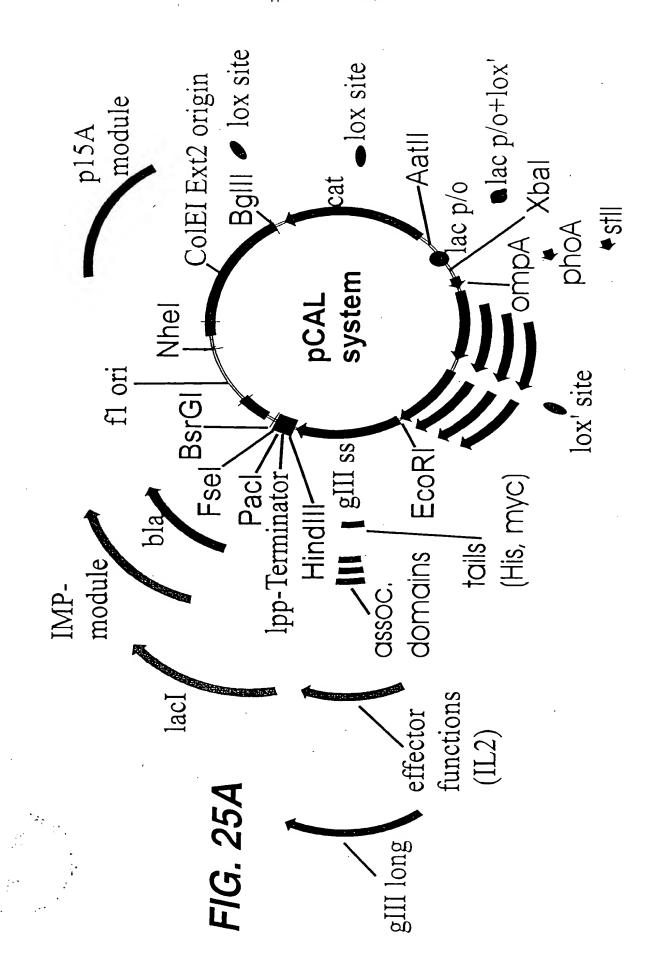
| FREQUEN   | Μ             | $\infty$      | 7            | $\leftarrow$  | $\vdash$     | $\vdash$      | ⊣        | $\leftarrow$ | $\leftarrow$ | IJ·      | 4                | $\leftarrow$ I |
|-----------|---------------|---------------|--------------|---------------|--------------|---------------|----------|--------------|--------------|----------|------------------|----------------|
| EOT       | Z             | M             | Z            | M             | M            | M             | ß        | Ż            | 3            | Z        | Z                | Z              |
| TOT       | >             | >             | X            | $\succ$       | >            | $\succ$       | $\succ$  | $\succ$      | $\succ$      | $\succ$  | $\triangleright$ | >              |
| TOT       | О             | О             | Ω            | О             | О            | О             | Ω        | П            | О            | П        | Ω                | Ω              |
| JOOE      | ſΤ            | $\Xi$         | ĮΤί          | Ĺτι           | $\Xi$        | $\Sigma$      | ı        | $\Xi$        | $\Xi$        | $\Xi$    | $\Xi$            | ſτι            |
| JOOD      | $\mathcal{O}$ | $\bowtie$     | 民            | Ĺτί           | 田            | $\boxtimes$   | 1        | 民            | >            | Ĺщ       | 団                | Z              |
| JOOT      | $\bowtie$     | 只             | $\bowtie$    | $\succ$       | $\mathbb{Z}$ | X             | 1        | $\bowtie$    | $\succ$      | 民        | X                | X              |
| TOOB      | 民             | 只             | $\Omega$     | 闰             | ഗ            | 民             | 1        | $\succ$      | >            | $\alpha$ | U                | $\alpha$       |
| Y00T      | $\vdash$      | Z             | Н            | Ω             | M            | 田             | 1        | Ĺτι          | $\circ$      | لئر      | 召                | $\Xi$          |
| 00 T      | K             | X             | Д            | Ы             | Ĺτι          | $\alpha$      | Д        | 3            | Ŋ            | 召        | Ŋ                | $\alpha$       |
| 66        | Ø             | ſΤι           | $\mathbb{Z}$ | 又             | Ω            | Д             | щ        | 耳            | M            | $\Sigma$ | 口                | $\Xi$          |
| 86        | $\geq$        | Ш             | $\Xi$        | $\mathbb{Z}$  | Ç            | 臼             | Ø        | Z            | $\Xi$        | Ø        | Ø                | Ц              |
| ۷6        | Д             | M             | M            | П             | M            | 니             | X        | E            | О            | O        | 口                | $\alpha$       |
| 96        | 民             | $\circ$       | 民            | ഗ             | Д            | $\Omega$      | $\Sigma$ | X            | X            | X        | $\Sigma$         | $\Sigma$       |
| <i>S6</i> | $\vdash$      | Z             | X            | $\succ$       | >            | Z             | Н        | 以            | $\mathbb{N}$ | Z        | Z                | Z              |
| Þ6        | 只             | $\alpha$      | 民            | 民             | $\alpha$     | $\alpha$      | 召        | 召            | $\alpha$     | 以        | 召                | 以              |
| CC        | $\mathcal{A}$ | $\mathcal{A}$ | ~            | $\mathcal{A}$ | ~            | $\mathcal{A}$ | ~        | ~            | ~            | ~        | ~                | ~              |

| •          |               |                 |               |                          |                |                 |
|------------|---------------|-----------------|---------------|--------------------------|----------------|-----------------|
| FREQUENCY  | ₽,            | $\sim$          | 7             | ٦                        | $\leftarrow$ I | $\leftarrow$    |
| EOT        | Z             | 3               | 3             | M                        | M              | 3               |
| <i>T05</i> | X             | $\succ$         | ≻ı            | $\triangleright$         | Y              | ×               |
| TOT        | Ω             | $\Box$          | Ω             | Ω                        | Ω              | Ω               |
| IOOE       | ĹΤι           | ĹŢ              | Ĺц            | ſц                       | Ĺτι            | ſц              |
| 100D       | K             | Ŏ               | O             | $\Xi$                    | 3              | $\circ$         |
| J00T       | Ы             | $\Sigma$        | $\Sigma$      | $\vdash$                 | $\asymp$       | $\Sigma$        |
| T00B       | $\times$      | $\bowtie$       | ×             | X                        | $\Xi$          | O               |
| AOOI       | 以             | O               | Z             | $\Sigma$                 | $\vdash$       | 民               |
| 00 T       | $\asymp$      | 3               | $\alpha$      | $\boxtimes$              | $\alpha$       | ഗ               |
| 66         | K             | $\triangleleft$ | Ø             | Ø                        | 民              | $\triangleleft$ |
| 86         | Ø             | 出               | $\succ$       | Ŋ                        | 니              | 召               |
| L6         | $\asymp$      | $\alpha$        | $\asymp$      | 以                        | Д              | $\bowtie$       |
| 96         | Н             | Z               | >             | $\asymp$                 | $\asymp$       | $\alpha$        |
| 56         | $\Rightarrow$ | $\succ$         | $\succ$       | · >-                     | $\alpha$       | $\succ$         |
| ħ6         | 異             | 召               | $\alpha$      | $\alpha$                 | $\alpha$       | 民               |
| 86         | Ø             | Ø               | K             | æ                        | Ø              | Ø               |
| 76         | $\mathcal{O}$ | $\mathcal{O}$   | $\mathcal{O}$ | $\overline{\mathcal{O}}$ | <u>U</u> .     | $\mathcal{O}$   |

| FREQUENCY | 16                       | H             | $\vdash$      | .П       | $\vdash$                 | $\leftarrow$     | $\leftarrow$ I | <del>, -  </del> |
|-----------|--------------------------|---------------|---------------|----------|--------------------------|------------------|----------------|------------------|
| EOI       | $\geq$                   | Z             | 3             | Z        | Z                        | 3                | B              | Z                |
| IOS       | >                        | $\rightarrow$ | $\succ$       | ×        | ×                        | $\triangleright$ | ×              | ≻₁               |
| TOT       | О                        | О             | О             | Д        | Ω                        | Ω                | $\Box$         | Ω                |
| JOOE      | Ĺц                       | $\Sigma$      | ſτι           | $\Sigma$ | $\Sigma$                 | Ĺ                | $\Sigma$       | Ĺι               |
| TOOD      | 耳                        | Д             | O             | 3        | >                        | ഗ                | 3              | Z                |
| J00T      | G                        | Ω             | >             | 工        | 田                        | $\circ$          | 口              | $\succ$          |
| TOOB      | ×                        | $\succ$       | 3             | 耳        | Ω                        | $\vdash$         | Z              | 3                |
| ¥00T      | Н                        | ഗ             | $\succ$       | വ        | $\alpha$                 | لتبا             | 口              | ш                |
| 00 T      | $\bowtie$                | Z             | Z             | ×        | Ø                        | $\circ$          | $\vdash$       | Н                |
| 66        | ഗ                        | ſщ            | О             | 니        | $\circ$                  | S                | Ø              | 口                |
| 86        | $\alpha$                 | П             | 니             | $\succ$  | Ш                        | Z                | Щ              | H                |
| ۷6        | $\succ$                  | $\alpha$      | П             | Ø        | Н                        | 江                | 口              | വ                |
| 96        | 異                        | $\geq$        | <b>A</b>      | O        | 니                        | Z                | Ω              | 3                |
| 56        | Ø                        | 1             | $\Sigma$      | ıП       | K                        | S                | >              | Ω                |
| ₽6        | 民                        | 民             | 公             | $\alpha$ | 民                        | $\alpha$         | K              | $\alpha$         |
| £6        | Ø                        | Ø             | Ø             | Ø        | Ø                        | æ                | K              | Ø                |
| 76        | $\overline{\mathcal{O}}$ | $\mathcal{O}$ | $\mathcal{O}$ | <u>ں</u> | $\overline{\mathcal{O}}$ | $\mathcal{O}$    | $\circ$        | $\circ$          |

| REQUENCY  | 4             | か        | 2        | <del>,</del>    | $\vdash$ | 2       | $\leftarrow$ I | 13            | т                | <del>,</del>  | $\leftarrow$  | <del></del> 1  |
|-----------|---------------|----------|----------|-----------------|----------|---------|----------------|---------------|------------------|---------------|---------------|----------------|
| EOI       | Z             | Z        | M        | Z               | Z        | 3       | M              | N             | ß                | M             | M             | 3              |
| ZOT       | ×             | >        | $\gt$    | $\succ$         | >        | $\succ$ | >-             | $\overline{}$ | $\triangleright$ | $\supset$     | X             | $\succ$        |
| TOT       | Ω             | О        | Д        | Ω               | Ω        | О       | $\Box$         | $\Box$        | О                | О             | Ω             | Ω              |
| JOOE      | 1             | ĮΤ       | $\Sigma$ | $\Sigma$        | $\Sigma$ | $\Xi$   | لتر            | ĹΤί           | $\Sigma$         | ſΤ            | i             | $\Sigma$       |
| JOOD      | ı             | $\alpha$ | $\circ$  | Н               | Ø        | О       | ×              | ×             | 召                | ĹŢ            | 1             | 니              |
| 100Ca     | ı             | 1        | i        | 1               | 以        | 1       | .1             | 1             | 1                | 1             | I             | ł              |
| 200T      | 1             | 吖        | $\alpha$ | 異               | $\alpha$ | 니       | 公              | 以             | Z                | 民             | 1             | 以              |
| IOOB      | I             | $\gt$    | W        | Н               | Д        | Н       | >              | 以             | Ω                | X             | I             | 異              |
| AOOI      | I             | لترا     | X        | $\triangleleft$ | Z        | $\Xi$   | Z              | ⊱             | 江                | S             | ŀ             | $\bigcirc$     |
| 00 T      | ГIJ           | ഗ        | S        | $\Omega$        | S        | $\Box$  | K              | X             | >                | $\times$      | لتر           | $\bowtie$      |
| 66        | [             | Д        | ഗ        | $\Rightarrow$   | K        | >       | ⊱              | ഗ             | $\succ$          | $\vdash$      | 口             | <del>[-1</del> |
| 86        | لتر           | 口        | 闰        | 口               | 口        | Z       | 口              | 口             | Ø                | 团             | $\Xi$         | 団              |
| 46        | Q             |          | X        | О               | ĹĻ       | 口       | ഗ              | $\times$      | [-1              | 又             | Н             | 口              |
| 96        | Гц            | لتا      | Ц        | O               | $\Xi$    | Z       | $\succ$        | Щ             | ×                | 3             | $\succ$       | Щ              |
| 56        | Ŋ             | $\circ$  | Н        | 口               | Z        | 口       | O              | O             | ×                | 召             | О             | Ø              |
| <i>ħ6</i> | 民             | 民        | 召        | 公               | 以        | DC,     | 民              | K             | 民                | 召             | $\alpha$      | 民              |
| 86        | Ø             | A        | Ø        | K               | Ø        | Ø       | <              | <             | Ø                | Ø             | Ø             | <              |
| 76        | $\mathcal{O}$ | $\circ$  | $\circ$  | $\mathcal{O}$   | ()       | $\circ$ | $\mathcal{O}$  | $\bigcirc$    | $\circ$          | $\mathcal{O}$ | $\mathcal{O}$ | $\mathcal{O}$  |

| FREQUENCY | Ŋ             | <del></del> 1 | $\leftarrow$  | <del></del>   | $\vdash$      | <del>~</del>  |
|-----------|---------------|---------------|---------------|---------------|---------------|---------------|
| EOT       | 3             | M             | M             | M             | M             | M             |
| IOS       | ≻             | $\supset$     | >             | >-            | $\rightarrow$ | >             |
| ΤΟΤ       | Ω             | О             | Ω             | Д             | О             | Ω             |
| JOOE      | $\Sigma$      | ĹĽ            | $\Sigma$      | $\Sigma$      | $\Sigma$      | ĹΤΊ           |
| T00D      | >             | $\alpha$      | 召             | O             | $\succ$       | ſτι           |
| JOOT      | $\succ$       | ſщ            | >             | S             | Z             | 工             |
| 100B      | Д             | $\Rightarrow$ | >             | Z             | Z             | $\vdash$      |
| AOOI      | Н             | Z             | 山             | ഗ             | വ             | 니             |
| 00 T      | Ø             | $\Rightarrow$ | $\Sigma$      | ıП            | Ø             | Д             |
| 66        | $\Rightarrow$ | $\Xi$         | $\circ$       | $\propto$     | Z             | X             |
| 86        | 口             | $\succ$       | 印             | $\succ$       | 民             | Ĺτι           |
| 46        | Ŋ             | ⊱             | Ĺц            | 口             | ഗ             | Ŋ             |
| 96        | Q             | Ĺц            | Щ             | X             | Д             | Ŋ             |
| 56        | О             | >             | >             | Щ             | $\succ$       | Ω             |
| Þ6        | 異             | $\alpha$      | 民             | 民             | 民             | 召             |
| E6        | K             | Ø             | Ø             | Þ             | Ø             | Ø             |
| 76        | $\mathcal{O}$ | $\mathcal{O}$ | $\mathcal{O}$ | $\mathcal{O}$ | $\mathcal{O}$ | $\mathcal{O}$ |



| unique restriction site | Isoschizomers                     |
|-------------------------|-----------------------------------|
| Aatll                   |                                   |
| AfIII                   | Bfrl, BspTl, Bst981               |
| Ascl                    | 1                                 |
| Asel                    | Vspl, Asnl, PshBl                 |
| BamHl                   | Bstl                              |
| Bbel                    | Ehel, Kasl, Narl                  |
| BbsI                    | BpuAl, Bpil                       |
| BgIII                   | 1                                 |
| Blpl                    | Bpu1102I,CellI, BlpI              |
| BsaBI                   | Maml, Bsh1365l, BsrBRl            |
| BsiWl                   | Pfl23II, Spll, Sunl               |
| BspEl                   | AccIII, BseAI, BsiMI, Kpn2I, Mrol |
| BsrGI                   | Bsp1407I, SspBI                   |
| BssHII                  | Paul                              |
| BstEII                  | BstPl, Eco91l, Eco0651            |
| BstXI                   |                                   |
| Bsu36l                  | Aocl, Cvnl, Eco811                |
| Dralll                  | 1                                 |
| DsmAl                   |                                   |
| Eagl                    | BstZl, EclXl, Eco52l, Xmalll      |
| Eco571                  | 1                                 |
| Eco01091                | Drall                             |
| EcoRI                   |                                   |
| EcoRV                   | Eco32I                            |
| Fsel                    | 1                                 |
| HindIII                 | <u> </u>                          |
| Hpal                    | 1                                 |
| Kpnl                    | Acc651, Asp7181                   |
| Mlul                    | 1                                 |
| Mscl                    | Ball, MluNl                       |

FIG. 25B

| unique restriction site | Isoschizomers                      |
|-------------------------|------------------------------------|
| Munl                    | Mfel                               |
|                         | 1                                  |
| Nhel                    |                                    |
| Nsil                    | Ppu10l, EcoT22l, Mph1103l          |
| NspV                    | Bsp119l, BstBl, Csp45l, Lspl, Sful |
| Pacl                    |                                    |
| Pmel                    | /                                  |
| PmII                    | BbrPl, Eco72l, PmaCl               |
| Psp5II                  | PpuMI                              |
| Pstl                    | /                                  |
| Rsrll                   | (Rsril), Cpol, Cspl                |
| SanDI                   |                                    |
| Sapl                    |                                    |
| SexAl                   |                                    |
| Spel                    | . /                                |
| Sfil                    |                                    |
| Sphl                    | Bbul, Pael, Nspl                   |
| Stul                    | Aatl, Eco147l                      |
| Styl                    | Eco130I, EcoT14I                   |
| Xbal                    | BspLU11II                          |
| Xhol                    | PaeR7I                             |
| Xmal                    | Aval, Smal, Cfr91, PspAl           |

FIG. 25C

|                                              | 1                                                    |                                                        | <del></del>                    |                                                                                                                                                          |
|----------------------------------------------|------------------------------------------------------|--------------------------------------------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| reference                                    | Skerra et al. (1991)<br>Bio/Technology 9,<br>273-278 | Hoess et al. (1986)<br>Nucleic Acids Res.<br>2287-2300 | see M2                         | Ge et al., (1994)<br>Expressing<br>antibodies in E.<br>coli. In: Antibody<br>engineering: A<br>practical approach.<br>IRL Press, New<br>York, pp 229-266 |
| template                                     | vector<br>pASK30                                     | (synthetic)                                            | (synthetic)                    | vector<br>plG10                                                                                                                                          |
| sites to be<br>inserted                      | Aatli                                                | lox, BgIII                                             | lox', Sphl                     | none                                                                                                                                                     |
| sites to be<br>removed                       | 2x Vspl<br>(Asel)                                    | 2x Vspl<br>(Asel)                                      | none                           | Sphl,<br>BamHl                                                                                                                                           |
| functional element                           | lac<br>promotor/operator                             | Cre/lox<br>recombination site                          | Cre/lox'<br>recombination site | glllp of filamentous<br>phage with N-<br>terminal<br>myctail/amber<br>codon                                                                              |
| module/flan-<br>king<br>restriction<br>sites | Aatii-lacp/o-<br>Xbai                                | BgIII-lox-<br>Aatii                                    | Xbal-lox'-<br>Sph1             | EcoRI-<br>gIIIlong-<br>HindIII                                                                                                                           |
| , ON                                         | M                                                    | M2                                                     | M3                             | M7-1                                                                                                                                                     |

# FIG. 26A

| ,      |                                |                                                                               |                                  |                      |                 |          |
|--------|--------------------------------|-------------------------------------------------------------------------------|----------------------------------|----------------------|-----------------|----------|
| M7-11  | M7-II EcoRI-gIIIss-<br>HindIII | truncated gillp of<br>filamentous phage<br>with N-terminal Gly-<br>Ser linker | Sphl                             |                      | vector<br>plG10 | see M7-I |
| M7-III | EcoRI-gIIIss-<br>HindIII       | truncated gillp of filamentous phage with N-terminal myctail/amber codon      | Sphl, Bbsl                       | ·                    | vector<br>pIG10 | see M7-1 |
| M8     | Sphl-lox-<br>HindIII           | Cre/lox<br>recombination site                                                 | none                             | xol                  | (synthetic)     | see M3   |
| M9-11  | HindIII-Ipp-<br>Pacl           | lpp-terminator                                                                | none                             | Pacl, Fsel           | (synthetic)     | see M1   |
| M10-   | Paci/Fsel-bla-<br>BsrGl        | beta-lactamase/bla<br>(ampR)                                                  | Vspl,<br>Eco571,<br>BssSl        | Pacl, Fsel,<br>BsrGl | pASK30          | see M1   |
| M11-   | BsrGI-f1 ori-<br>Nhel          | origin of single-<br>stranded replication                                     | Dralll<br>(Banll not<br>removed) | BsrGl, Nhel          | pASK30          | see M1   |
| M11-   | BsrGI-f1 ori-<br>Nhel          | origin of single-<br>stranded replication                                     | Oralli,<br>Banli                 | BsrGI, Nhel          | pASK30          | see M1   |

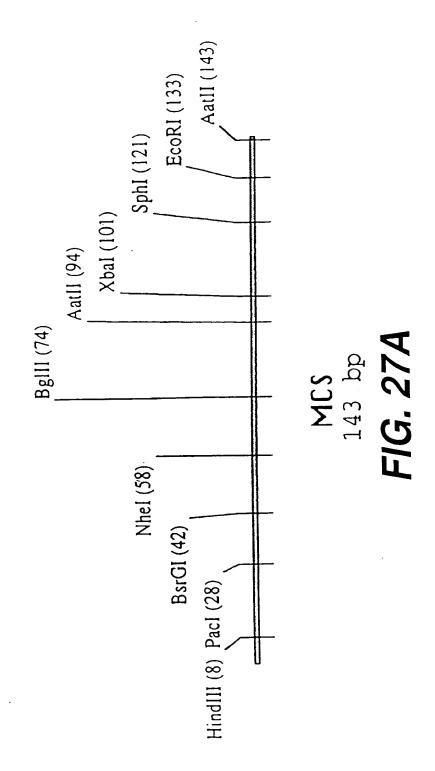
### FIG. 26B

|                                                    | ,                             | ·                                              | ····                                                                       | 1                                   |                                                                         |
|----------------------------------------------------|-------------------------------|------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------|-------------------------------------------------------------------------|
| Rose, R.E. (1988)<br>Nucleic Acids Res.<br>16, 355 | see M3                        | Yanisch-Peron, C.<br>(1985) Gene<br>33,103-119 | Cardoso, M. &<br>Schwarz,S. (1992)<br>J. Appl<br>Bacteriol.72, 289-<br>293 | see M1                              | Knappik, A &<br>Plückthun, A.<br>(1994)<br>BioTechniques 17,<br>754-761 |
| Nhel, BgIII pACYC184                               | (synthetic)                   | pUC19                                          | pACYC184                                                                   | (synthetic)                         | (synthetic)                                                             |
| Nhel, BgIII                                        | BgIII, Iox,<br>Xmnl           | Bgill, Nhel                                    |                                                                            |                                     |                                                                         |
| BssSI, VspI,<br>NspV                               | none                          | Eco571<br>(BssSI not<br>removed)               | BspEI, MscI,<br>Styl/Ncol                                                  | (synthetic)                         | (synthetic)                                                             |
| origin of double-<br>stranded replication          | Cre/lox<br>recombination site | origin of double-<br>stranded replication      | chloramphenicol-<br>acetyltransferase/<br>cat (camR)                       | signal sequence of<br>phosphatase A | signal sequence of<br>phosphatase A +<br>FLAG detection tag             |
| Nhel-p15A-<br>Bgill                                | BgIII-lox-<br>BgIII           | BgIII-ColEI-<br>Nhel                           | Aatil-cat-<br>Bgill                                                        | Xbal-phoA-<br>EcoRI                 | Xbal-phoA-<br>FLAG-EcoRI                                                |
| M12                                                | M13                           | M14-<br>Ext2                                   | M17                                                                        | M19                                 | M20                                                                     |

# FIG. 26C

| Ž.  |                           |                                                              |                                                                  |                 |                                                                                               |
|-----|---------------------------|--------------------------------------------------------------|------------------------------------------------------------------|-----------------|-----------------------------------------------------------------------------------------------|
| M21 | Xbal-stll-<br>Sapl        | heat-stable<br>enterotoxin II signal (synthetic)<br>sequence | (synthetic)                                                      | <br>(synthetic) | Lee et al. (1983)<br>Infect. Immunol.<br>264-268                                              |
| M41 | AfIII-laci-<br>Nhel       | lac-repressor                                                | BstXI,<br>MluI,BbsI,<br>BanII,<br>BstEII,<br>HpaI, BbeI,<br>VspI | pASK30          | see M1                                                                                        |
| M42 | EcoRI-Histail-<br>HindIII | poly-histidine tail                                          | (synthetic)                                                      | (synthetic)     | Lindner et al.,<br>(1992) Methods: a<br>companion to<br>methods in<br>enzymology 4, 41-<br>56 |

### FIG. 26D



|              | HindIll                                   | 7.1                                                | A<br>C<br>C                                                          | DALGI                                                                                        |
|--------------|-------------------------------------------|----------------------------------------------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| $\leftarrow$ | ACATGTAAGC<br>TGTACATTCG                  | TTCCCCCCCC                                         | ACATGTAAGC TTCCCCCCCC CCTTAATTAA<br>TGTACATTCG AAGGGGGGGG GGAATTAATT | ACATGTAAGC TTCCCCCCC CCTTAATTAA CCCCCCCCC TGTACACCCC                                         |
| 51           | Nhel<br>CCCCCGCTA GC                      | Nhel<br>cccccccra gcccccccc<br>gggggggar cgggggggg | Bglii<br>CCAGATCTCC<br>GGTCTAGAGG                                    | Aatii Xbai<br>CCCCCCGA CGTCCCCCT<br>GGGGGGCT GCAGGGGGGA                                      |
| 101          | XbaI<br>~~~~~<br>CTAGACCCCC<br>GATCTGGGGG | Sphi<br>ccccccarc c                                | 9999999999999999<br>                                                 | xbai EcoRI Aatli TAASA ECORI AATII CTAGACCCCC CCCCCCCCCC CGAATTCGAC GTC GATCTGGGG GGGGGGGGGG |

FIG. 27B

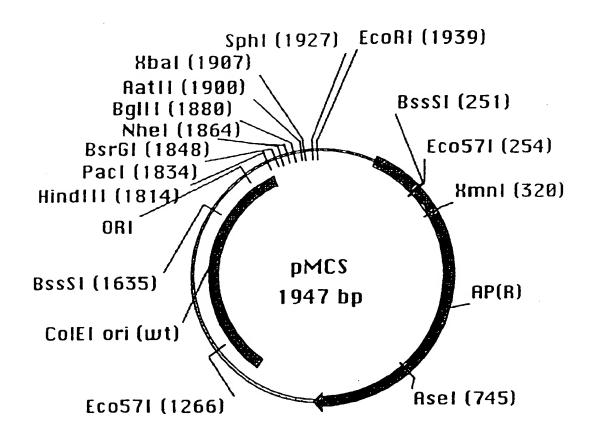


FIG. 28A

| ATCCTTGAGA                        | CAGCGGTAAG               | TGGATCTCAA<br>ACCTAGAGTT | TACATCGAAC<br>ATGTAGCTTG | ACGAGTGGGT<br>TGCTCACCCA | 251          |
|-----------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------|
| ł                                 | •                        |                          |                          |                          |              |
| AGTTGGGTĞC<br>TCAACCCACG<br>BSSSI | GCTGAAGATC<br>CGACTTCTAG | AGTAAAAGAT<br>TCATTTTCTA | CGCTGGTGAA<br>GCGACCACTT | CACCCAGAAA<br>GTGGGTCTTT | 201          |
|                                   | Eco57I                   |                          |                          |                          |              |
| TGTTTTTGCT<br>ACAAAAACGA          | TTTGCCTTCC<br>AAACGGAAGG | TTTGCGGCAT<br>AAACGCCGTA | TATTCCCTTT<br>ATAAGGGAAA | GTGTCGCCCT               | 151          |
| CAACATTTCC<br>GTTGTAAAGG          | TATGAGTATT<br>ATACTCATAA | AAAGGAAGAG<br>TTTCCTTCTC | TAATATTGAA<br>ATTATAACTT | AATGCTTCAA<br>TTACGAAGTT | 101          |
| AACCCTGATA<br>TTGGGACTAT          | ATGAGACAAT<br>TACTCTGTTA | GTATCCGCTC<br>CATAGGCGAG | ATTCAAATAT<br>TAAGTTTATA | TTCTAAATAC<br>AAGATTTATG | 51           |
| TTGTTTATTT<br>AACAAATAAA          | GAACCCCTAT<br>CTTGGGGATA | AATGTGCGCG<br>TTACACGCGC | TTTTCGGGGA               | CAGGTGGCAC<br>GTCCACCGTG | $\leftarrow$ |

FIG. 28B

BSSSI

### XmnI

| 301 | GTTTTCGCCC<br>CAAAAGCGGG | CGAAGAACGT<br>GCTTCTTGCA | TTTCCAATGA               | TGAGCACTTT<br>ACTCGTGAAA | TAAAGTTCTG<br>ATTTCAAGAC |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 351 | CTATGTGGCG               | CGGTATTATC               | CCGTATTGAC               | GCCGGGCAAG               | AGCAACTCGG               |
|     | GATACACCGC               | GCCATAATAG               | GGCATAACTG               | CGGCCCGTTC               | TCGTTGAGCC               |
| 401 | TCGCCGCATA               | CACTATTCTC<br>GTGATAAGAG | AGAATGACTT<br>TCTTACTGAA | GGTTGAGTAC<br>CCAACTCATG | TCACCAGTCA               |
| 451 | CAGAAAAGCA               | TCTTACGGAT               | GGCATGACAG               | TAAGAGAATT               | ATGCAGTGCT               |
|     | GTCTTTTCGT               | AGAATGCCTA               | CCGTACTGTC               | ATTCTCTTAA               | TACGTCACGA               |
| 501 | GCCATAACCA               | TGAGTGATAA               | CACTGCGGCC               | AACTTACTTC               | TGACAACGAT               |
|     | CGGTATTGGT               | ACTCACTATT               | GTGACGCCGG               | TTGAATGAAG               | ACTGTTGCTA               |
| 551 | CGGAGGACCG               | AAGGAGCTAA               | CCGCTTTTTT               | GCACAACATG               | GGGGATCATG               |
|     | GCCTCCTGGC               | TTCCTCGATT               | GGCGAAAAAA               | CGTGTTGTAC               | CCCCTAGTAC               |
| 601 | TAACTCGCCT               | TGATCGTTGG               | GAACCGGAGC               | TGAATGAAGC               | CATACCAAAC               |
|     | ATTGAGCGGA               | ACTAGCAACC               | CTTGGCCTCG               | ACTTACTTCG               | GTATGGTTTG               |
| 651 | GACGAGCGTG               | ACACCACGAT               | GCCTGTAGCA               | ATGGCAACAA               | CGTTGCGCAA               |

### FIG. 28C

| GCAACGCGTT                 |
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| CAATTAATAG | CTCGGCCCTT | AGCGTGGGTC | TCCCGTATCG | ACGAAATAGA | AACTGTCAGA | CATTTTAAT  |
|------------|------------|------------|------------|------------|------------|------------|
| GTTAATATC  |            | TCGCACCCAG | AGGCATAGC  | TGCTTTATCT | TTGACAGTCT | GTAAAAATTA |
| TTCCCGGCAA | CACTTCTGCG | GGAGCCGGTG | TGGTAAGCCC | CTATGGATGA | AAGCATTGGT | TTTAAAACTT |
|            | GTGAAGACGC | CCTCGGCCAC | ACCATTCGGG | GATACCTACT | TTCGTAACCA | AAATTTTGAA |
| TTACTCTAGC | GTTGCAGGAC | TGATAAATCT | TGGGGCCAGA | AGTCAGGCAA | CTCACTGATT | TTTAGATTGA |
| AATGAGATCG | CAACGTCCTG | ACTATTTAGA | ACCCCGGTCT | TCAGTCCGTT | GAGTGACTAA | AAATCTAACT |
| GGCGAACTAC | GGCGGATAAA | GGTTTATTGC | ATTGCAGCAC | CACGACGGGG | AGATAGGTGC | TCATATATAC |
| CCGCTTGATG | CCGCCTATTT | CCAAATAACG | TAACGTCGTG | GTGCTGCCCC | TCTATCCACG | AGTATATATG |
| ACTATTAACT | ACTGGATGGA | CCGGCTGGCT | TCGCGGTATC | TAGTTATCTA | CAGATCGCTG | CCAAGTTTAC |
| TGATAATTGA | TGACCTACCT | GGCCGACCGA | AGCGCCATAG | ATCAATAGAT | GTCTAGCGAC | GGTTCAAATG |
| 701        | 751        | 801        | 851        | 901        | 951        | 1001       |

### FIG. 28D

| 4051 | TTAAAAGGAT               | CTAGGTGAAG              | ATCCTTTTTG                     | ATAATCTCAT                             | GACCAAAATC               |
|------|--------------------------|-------------------------|--------------------------------|----------------------------------------|--------------------------|
|      | AATTTTCCTA               | GATCCACTTC              | TAGGAAAAAC                     | TATTAGAGTA                             | CTGGTTTTAG               |
| 1101 | CCTTAACGTG               | AGTTTTCGTT              | CCACTGAGCG                     | TCAGACCCCG                             | TAGAAAAGAT               |
|      | GGAATTGCAC               | TCAAAAGCAA              | GGTGACTCGC                     | AGTCTGGGGC                             | ATCTTTTCTA               |
| 1151 | CAAAGGATCT               | TCTTGAGATC              | CTTTTTTTCT                     | GCGCGTAATC                             | TGCTGCTTGC               |
|      | GTTTCCTAGA               | AGAACTCTAG              | GAAAAAAAGA                     | CGCGCATTAG                             | ACGACGAACG               |
| 1201 | AAACAAAAAA               | ACCACCGCTA              | CCAGCGGTGG                     | TTTGTTTGCC                             | GGATCAAGAG               |
|      | TTTGTTTTT                | TGGTGGCGAT              | GGTCGCCACC                     | AAACAAACGG                             | CCTAGTTCTC               |
| 1251 | CTACCAACTC<br>GATGGTTGAG | TTTTCCGAA<br>AAAAAGGCTT | GGTAACTGGC<br>CCATTGACCG<br>EC | C TTCAGCAGAG<br>G AAGTCGTCTC<br>Eco57I | CGCAGATACC<br>GCGTCTATGG |
| 1301 | AAATACTGTC               | CTTCTAGTGT              | AGCCGTAGTT                     | T AGGCCACCAC                           | TTCAAGAACT               |
|      | 'ITTATGACAG              | GAAGATCACA              | TCGGCATCAA                     | A TCCGGTGGTG                           | AAGTTCTTGA               |

### FIG. 28E

ACCAGTGGCT TGGTCACCGA

CTGTAGCACC GCCTACATAC CTCGCTCTGC TAATCCTGTT GACATCGTGG CGGATGTATG GAGCGAGACG ATTAGGACAA

1351

| 1401 | GCTGCCAGTG               | GCGATAAGTC<br>CGCTATTCAG | ĠTGTCTTACC<br>CACAGAATGG | GGGTTGGACT<br>CCCAACCTGA          | CAAGACGATA<br>GTTCTGCTAT |
|------|--------------------------|--------------------------|--------------------------|-----------------------------------|--------------------------|
| 1451 | GTTACCGGAT               | AAGGCGCAGC               | GGTCGGGCTG               | AACGGGGGGT                        | TCGTGCACAC               |
|      | CAATGGCCTA               | TTCCGCGTCG               | CCAGCCCGAC               | TTGCCCCCCA                        | AGCACGTGTG               |
| 1501 | AGCCCAGCTT               | GGAGCGAACG               | ACCTACACCG               | AACTGAGATA                        | CCTACAGCGT               |
|      | TCGGGTCGAA               | CCTCGCTTGC               | TGGATGTGGC               | TTGACTCTAT                        | GGATGTCGCA               |
| 1551 | GAGCTATGAG               | AAAGCGCCAC               | GCTTCCCGAA               | GGGAGAAAGG                        | CGGACAGGTA               |
|      | CTCGATACTC               | TTTCGCGGTG               | CGAAGGGCTT               | CCCTCTTTCC                        | GCCTGTCCAT               |
| 1601 | TCCGGTAAGC<br>AGGCCATTCG | GGCAGGGTCG<br>CCGTCCCAGC | GAACAGGAGA<br>CTTGTCCTCT | GCGCACGAGG<br>CGCGTGCTCC<br>BSSSI | GAGCTTCCAG<br>CTCGAAGGTC |
| 1651 | GGGGAAACGC               | CTGGTATCTT               | TATAGTCCTG               | TCGGGTTTCG                        | CCACCTCTGA               |
|      | CCCCTTTGCG               | GACCATAGAA               | ATATCAGGAC               | AGCCCAAAGC                        | GGTGGAGACT               |
| 1701 | CTTGAGCGTC<br>GAACTCGCAG | GATTTTTGTG<br>CTAAAAACAC | ATGCTCGTCA<br>TACGAGCAGT | GGGGGGGGA                         | GCCTATGGAA<br>CGGATACCTT |
| 1751 | AAACGCCAGC               | AACGCGGCCT               | TTTTACGGTT               | CCTGGCCTTT                        | TGCTGGCCTT               |

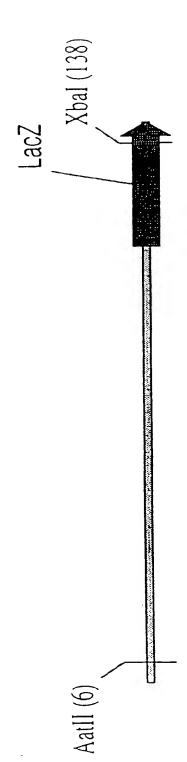
FIG. 28F

| RI                                       | ECORI                                                                                                            | Sphi                         | 1                                                   | XbaI                                   |      |
|------------------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------------------------------|----------------------------------------|------|
| Aatii<br>~~~~~<br>CCCCACGTC<br>GGGCTGCAG | BsrGI Nhel Bglil Aatii  CACCCCCCC CCGCTAGCCC CCCCCCCAG ATCTCCCCCC CCCCGACGTC GTGGGGGGGG GGGGGGGGGGGGGGGGGGGGGGGG | BG<br>CCCCCCCAG<br>GGGGGGGTC | Nhel<br>~~~~~~<br>CCGCTAGCCC<br>GGCGATCGGG          | BsrGI<br>~~<br>CACCCCCCC<br>GTGGGGGGGG | 1851 |
| BsrGI<br>~~~~<br>CCCCCTGTA<br>GGGGGACAT  | HindIII  ZZZZZZZZZZZZZZZZZZZZZZZZZZZZZZZZZ                                                                       | CCCCCCCTT                    | HindIII TTGCTCACAT GTAAGCTTCC AACGAGTGTA CATTCGAAGG | TTGCTCACAT                             | 1801 |
| ACGACCGGAA                               | TTTGCGGTCG TTGCGCCGGA AAAATGCCAA GGACCGGAAA ACGACCGGAA                                                           | AAAATGCCAA                   | T.T.GC.GCC.GGA                                      | 50,1.99091.1.1                         |      |

## FIG. 28G

CCCCCCGAA TTCACGT GGGGGGGCTT AAGTGCA

1901



M1 142 bp *FIG. 29A* 

Aatii

CCGAAATGTG CTCACTCATT AGGCACCCCA GGCTTTACAC GAGTGAGTAA TCCGTGGGGT TGTGAGTTAG ACACTCAATC CTGCAGAATT GACGTCTTAA

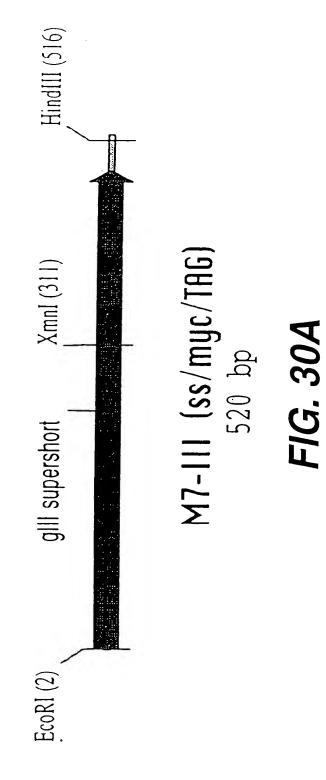
GATAACAATT CTATTGTTAA CGGCTCGTAT GTTGTGTGGA ATTGTGAGCG GCCGAGCATA CAACACACCT TAACACTCGC AAATACGAAG TTTATGCTTC 51

XbaI

CGAATTTCTA GCTTAAAGAT TCACACAGGA AACAGCTATG ACCATGATTA AGTGTGTCCT TTGTCGATAC TGGTACTAAT

101

FIG. 29B



| GTGGTGGCTC | AATAAGGGGG               | CGCTAAAGGC               | ATGGTTTCAT               | GGTGATTTTG               | TAATTCACCT |      |
|------------|--------------------------|--------------------------|--------------------------|--------------------------|------------|------|
| CACCACCGAG | TTATTCCCCC               | GCGATTTCCG               | TACCAAAGTA               | CCACTAAAAC               | ATTAAGTGGA |      |
| GATCTGTAGG | GGCAAACGCT               | TACAGTCTGA               | GCTGCTATCG               | TGGTGCTACT               | GTGACGGTGA |      |
| CTAGACATCC | CCGTTTGCGA               | ATGTCAGACT               | CGACGATAGC               | ACCACGATGA               | CACTGCCACT |      |
| CTCTGAGGAG | ATGAAAAGAT               | GAAAACGCGC               | TGATTACGGT               | CTAATGGTAA               | GCTCAAGTCG |      |
| GAGACTCCTC | TACTTTTCTA               | CTTTTGCGCG               | ACTAATGCCA               | GATTACCATT               | CGAGTTCAGC |      |
| AGAAGCTGAT | GATTTTGATT               | AAATGCCGAT               | CTGTCGCTAC               | TCCGGCCTTG               | TTCCCAAATG | Ħ    |
| TCTTCGACTA | CTAAAACTAA               | TTTACGGCTA               | GACAGCGATG               | AGGCCGGAAC               | AAGGGTTTAC |      |
| GAATTCGAGC | TGGTTCCGGT<br>ACCAAGGCCA | CTATGACCGA<br>GATACTGGCT | AAACTTGATT<br>TTTGAACTAA | TGGTGACGTT<br>ACCACTGCAA | CTGGCTCTAA | CumX |

201

151

251

EcoRI

 $\vdash$ 

51

101

# FIG. 30B

ATTTCCGTCA ATATTTACCT TCCCTCCCTC AATCGGTTGA TAAAGGCAGT TATAAATGGA AGGGAGGGAG TTAGCCAACT

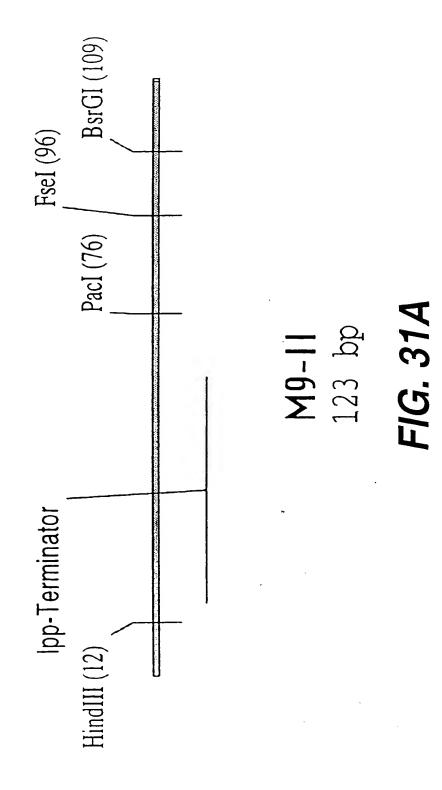
11111

TTAATGAATA AATTACTTAT

301

| GGAA TTTTCTATTG                             | CGTT TCTTTTATAT                             | GTTGCCACCT TTATGTATGT ATTTTCTACG TTTGCTAACA TACTGCGTAA               |                                               |
|---------------------------------------------|---------------------------------------------|----------------------------------------------------------------------|-----------------------------------------------|
| ACTT AAAAGATAAC                             | SCAA AGAAAATATA                             | CAACGGTGGA AATACATACA TAAAAGATGC AAACGATTGT ATGACGCATT               |                                               |
| ACCAIAIGAA<br>TGGTATACTT                    | TCTTTG                                      | TTTGCTAACA<br>AAACGATTGT                                             |                                               |
| ATGTCGCCCT TTTGTCTTTG GCGCTGGTAA ACCATATGAA | ATTGTGACAA AATAAACTTA TTCCGTGGTG TCTTTGCGTT | ATTTTCTACG                                                           |                                               |
| TACAGCGGGA AAACAGAAAC CGCGACCATT TGGTATACTT | TAACACTGTT TTATTTGAAT AAGGCACCAC AGAAACGCAA | TAAAAGATGC                                                           |                                               |
| TTTGTC1"1"1"G<br>AAACAGAAAC                 | AATAAACTTA<br>TTATTTGAAT                    | GTTGCCACCT TTATGTATGT ATTTTCTACG<br>CAACGGTGGA AATACATACA TAAAAGATGC | HindIII<br>GTCT TGATAAGCTT<br>CAGA ACTATTCGAA |
| ATGTCGCCCT TTTGTCTTTG                       | ATTGTGACAA                                  | GTTGCCACCT                                                           | TAAGGAGTCT                                    |
| TACAGCGGGA AAACAGAAAC                       | TAACACTGTT                                  | CAACGGTGGA                                                           | ATTCCTCAGA                                    |
| 351                                         | 401                                         | 451                                                                  | 501                                           |

FIG. 30C



### HindIII

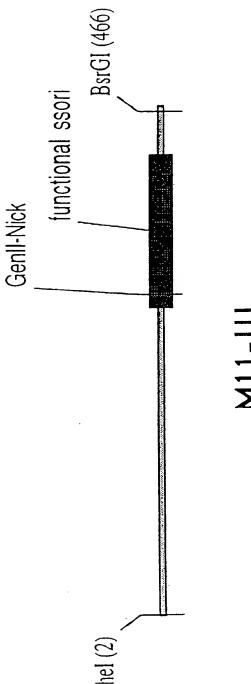
| AAATGGCGC AGATTGTGCG              | CCCCCCCCC TTCGAACTGG ACACTTCACT TTTTACCGCG TCTAACACGC |
|-----------------------------------|-------------------------------------------------------|
| AAAATGGCGC P                      | TTTTACCGCG TCTA                                       |
| TGTGAAGTGA AA                     | TGG ACACTTCACT                                        |
| AAGCTTGACC                        | TTCGAACTGG                                            |
| GGGGGGGG AAGCTTGACC TGTGAAGTGA AA | CCCCCCCCC TTCGAAC                                     |

| FseI | * * * * * * * * * * * * * * * * * * * * | 5540055005 55555555 5 |
|------|-----------------------------------------|-----------------------|
| PacI | ?<br>?<br>?<br>?<br>?                   | TTAATTAAAG            |
|      |                                         | TGTCTGCCGT            |
|      |                                         | ACATTTTTT             |
|      |                                         |                       |

S

TGTAAAAAA ACAGACGGCA AATTAATTTC CCCCCCCCC CGGCCGGACC GGGGGGTGT ACAGGGGGGG GGG CCCCCCCACA TGTCCCCCCC CCC BsrGI 101

FIG. 31B



M11-III 470 bp *FIG. 32A* 

|               | יין ער ד                 |                          |                          |                          |                          |
|---------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| <del></del> 1 | GCTAGCACGC               | GCCCTGTAGC<br>CGGGACATCG | GGCGCATTAA<br>CCGCGTAATT | 222522525<br>25255252525 | TGTGGTGGTT               |
| 51            | ACGCGCAGCG               | TGACCGCTAC               | ACTTGCCAGC               | GCCCTAGCGC               | CCGCTCCTTT               |
|               | TGCGCGTCGC               | ACTGGCGATG               | TGAACGGTCG               | CGGGATCGCG               | GGCGAGGAAA               |
| 101           | CGCTTTCTTC<br>GCGAAAGAAG | CCTTCCTTTC<br>GGAAGGAAAG | TCGCCACGTT<br>AGCGGTGCAA | CGCCGGCTTT               | CCCCGTCAAG<br>GGGCCAGTTC |
| 151           | CTCTAAATCG               | GGGCATCCCT               | TTAGGGTTCC               | GATTTAGTGC               | TTTACGGCAC               |
|               | GAGATTTAGC               | CCCGTAGGGA               | AATCCCAAGG               | CTAAATCACG               | AAATGCCGTG               |
| 201           | CTCGACCCCA               | AAAAACTTGA               | TTAGGGTGAT               | GGTTCTCGTA               | GTGGGCCATC               |
|               | GAGCTGGGGT               | TTTTTGAACT               | AATCCCACTA               | CCAAGAGCAT               | CACCCGGTAG               |
| 251           | GCCCTGATAG               | ACGGTTTTTC               | GCCCTTTGAC               | GTTGGAGTCC               | ACGTTCTTTA               |
|               | CGGGACTATC               | TGCCAAAAAG               | CGGGAAACTG               | CAACCTCAGG               | TGCAAGAAAT               |
| 301           | ATAGTGGACT               | CTTGTTCCAA               | ACTGGAACAA               | CACTCAACCC               | TATCTCGGTC               |
|               | TATCACCTGA               | GAACAAGGTT               | TGACCTTGTT               | GTGAGTTGGG               | ATAGAGCCAG               |
| 351           | TATTCTTTG                | ATTTATAAGG               | GATTTTGCCG               | ATTTCGGCCT               | ATTGGTTAAA               |

## FIG. 32B

ATAAGAAAAC TAAATATTCC CTAAAACGGC TAAAGCCGGA TAACCAATTT GAATTTTAAC AAAATATTAA CTTAAAATTG TTTTATAATT ATTTAACAAA AATTTAACGC TAAATTGTTT TTAAATTGCG AAATGAGCTG / 401

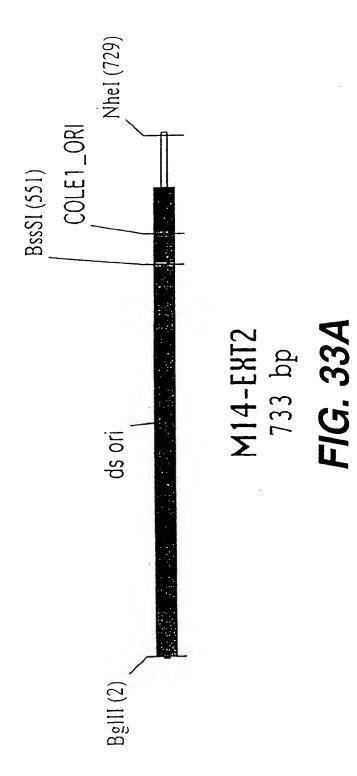
BsrGI

H 1

CGTTTACAAT TTCATGTACA GCAAATGTTA AAGTACATGT

451

FIG. 32C



|              | 4 4 6 7    |            |            |            |            |
|--------------|------------|------------|------------|------------|------------|
| $\leftarrow$ | AGATCTGACC | AAAATCCCTT | AACGTGAGTT | TTCGTTCCAC | TGAGCGTCAG |
|              | TCTAGACTGG | TTTTAGGGAA | TTGCACTCAA | AAGCAAGGTG | ACTCGCAGTC |
| 51           | ACCCCGTAGA | AAAGATCAAA | GGATCTTCTT | GAGATCCTTT | TTTTCTGCGC |
|              | TGGGGCATCT | TTTCTAGTTT | CCTAGAAGAA | CTCTAGGAAA | AAAAGACGCG |
| 101          | GTAATCTGCT | GCTTGCAAAC | AAAAAACCA  | CCGCTACCAG | CGGTGGTTTG |
|              | CATTAGACGA | CGAACGTTTG | TTTTTTGGT  | GGCGATGGTC | GCCACCAAAC |
| 151          | TTTGCCGGAT | CAAGAGCTAC | CAACTCTTTT | TCCGAAGGTA | ACTGGCTACA |
|              | AAACGGCCTA | GTTCTCGATG | GTTGAGAAAA | AGGCTTCCAT | TGACCGATGT |
| 201          | GCAGAGCGCA | GATACCAAAT | ACTGTTCTTC | TAGTGTAGCC | GTAGTTAGGC |
|              | CGTCTCGCGT | CTATGGTTTA | TGACAAGAAG | ATCACATCGG | CATCAATCCG |
| 251          | CACCACTTCA | AGAACTCTGT | AGCACCGCCT | ACATACCTCG | CTCTGCTAAT |
|              | GTGGTGAAGT | TCTTGAGACA | TCGTGGCGGA | TGTATGGAGC | GAGACGATTA |
| 301          | CCTGTTACCA | GTGGCTGCTG | CCAGTGGCGA | TAAGTCGTGT | CTTACCGGGT |
|              | GGACAATGGT | CACCGACGAC | GGTCACCGCT | ATTCAGCACA | GAATGGCCCA |
| 351          | TGGACTCAAG | ACGATAGTTA | CCGGATAAGG | CGCAGCGGTC | GGGCTGAACG |

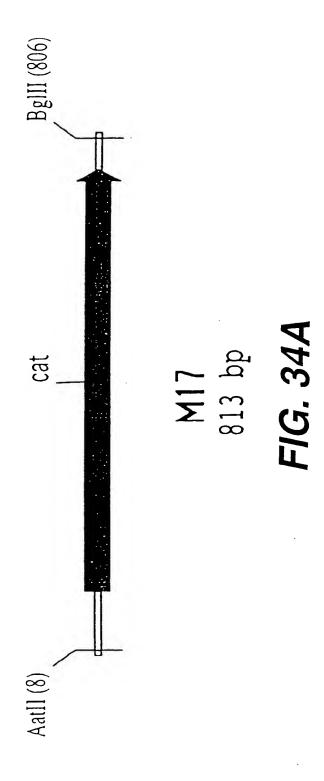
FIG. 33B

| SAGTTC TGCTATCAAT GGCCTATTCC GCGTCGCCAG CCCGACTTGC | STTCGT GCACACAGCC CAGCTTGGAG CGAACGACCT ACACCGAACT<br>SAAGCA CGTGTGGG GTCGAACCTC GCTTGCTGGA TGTGGCTTGA | PACCTA CAGCGTGAGC TATGAGAAAG CGCCACGCTT CCCGAAGGGAATGGAT GTCGCAGTCG ATACTCTTTC GCGGTGCGAA GGGCTTCCCT | SGCGGA CAGGTATCCG GTAAGCGGCA GGGTCGGAAC AGGAGAGCGC<br>CCGCCT GTCCATAGGC CATTCGCCGT CCCAGCCTTG TCCTCGCG<br>BSSSI | GGGAGC TTCCAGGGGG AAACGCCTGG TATCTTTATA GTCCTGTCGG<br>CCCTCG AAGGTCCCCC TTTGCGGACC ATAGAAATAT CAGGACAGCC<br>[ | CGCCAC CTCTGACTTG AGCGTCGATT TTTGTGATGC TCGTCAGGGG<br>GCGGTG GAGACTGAAC TCGCAGCTAA AAACACTACG AGCAGTCCCC | SAGCCT ATGGAAAAC GCCAGCAACG CGGCCTTTTT ACGGTTCCTG |
|----------------------------------------------------|--------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| ACCTGAGTTC TGCTATCA                                | GGGGGTTCGT GCACACAG<br>CCCCCAAGCA CGTGTGTC                                                             | GAGATACCTA CAGCGTGA<br>CTCTATGGAT GTCGCA                                                             | GAAAGGCGGA CAGGTATC<br>CTTTCCGCCT GTCCATAG                                                                      | ACGAGGGAGC TTCCAGGG<br>TGCTCCCTCG AAGGTCCC<br>BssSI                                                           | GTTTCGCCAC CTCTGACT                                                                                      | GGCGGAGCCT ATGGAAAA                               |
|                                                    | 401                                                                                                    | 451                                                                                                  | 501                                                                                                             | 551                                                                                                           | 601                                                                                                      | 651                                               |

FIG. 33C

NheI

GCCTTTTGCT GGCCTT1.GC TCACATGGCT AGC CGGAAAACGA CCGGAAAACG AGTGTACCGA TCG 701



| 1 | AALII |  |
|---|-------|--|

|               | ?<br>?<br>?              |                          |                          |                          |                          |
|---------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| <del></del> 1 | GGGACGTCGG               | GTGAGGTTCC               | AACTTTCACC               | ATAATGAAAT               | AAGATCACTA               |
|               | CCCTGCAGCC               | CACTCCAAGG               | TTGAAAGTGG               | TATTACTTTA               | TTCTAGTGAT               |
| 51            | CCGGGCGTAT               | TTTTTGAGTT<br>AAAAACTCAA | ATCGAGATTT<br>TAGCTCTAAA | TCAGGAGCTA<br>AGTCCTCGAT | AGGAAGCTAA<br>TCCTTCGATT |
| 101           | AATGGAGAAA               | AAAATCACTG               | GATATACCAC               | CGTTGATATA               | TCCCAATGGC               |
|               | TTACCTCTTT               | TTTTAGTGAC               | CTATATGGTG               | GCAACTATAT               | AGGGTTACCG               |
| 151           | ATCGTAAAGA<br>TAGCATTTCT | ACATTTTGAG<br>TGTAAAACTC | GCATTTCAGT<br>CGTAAAGTCA | CAGTTGCTCA               | ATGTACCTAT<br>TACATGGATA |
| 201           | AACCAGACCG               | TTCAGCTGGA               | TATTACGGCC               | TTTTTAAAGA               | CCGTAAAGAA               |
|               | TTGGTCTGGC               | AAGTCGACCT               | ATAATGCCGG               | AAAATTTCT                | GGCATTTCTT               |
| 251           | AAATAAGCAC               | AAGTTTTATC               | CGGCCTTTAT               | TCACATTCTT               | GCCCGCCTGA               |
|               | TTTATTCGTG               | TTCAAAATAG               | GCCGGAAATA               | AGTGTAAGAA               | CGGGCGGACT               |
| 301           | TGAATGCTCA               | CCCGGAGTTC               | CGTATGGCAA               | TGAAAGACGG               | TGAGCTGGTG               |
|               | ACTTACGAGT               | GGGCCTCAAG               | GCATACCGTT               | ACTTTCTGCC               | ACTCGACCAC               |
| 351           | ATATGGGATA               | GTGTTCACCC               | TTGTTACACC               | GTTTTCCATG               | AGCAAACTGA               |

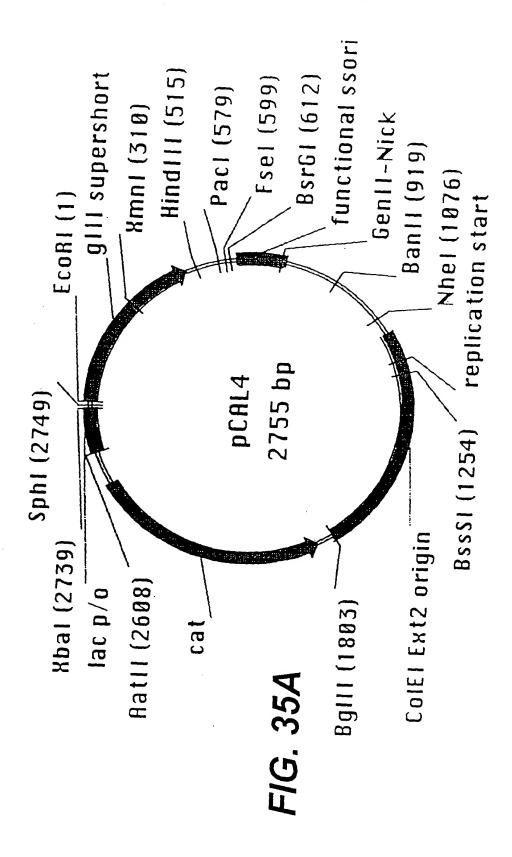
## FIG. 34B

| AAACGCCTGG               | GGGTGCCCTT               | GGCAGTTATT               | ATTTTTAA                 | GCGGGGCGTA               | 751 |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----|
| GAGTGGCAGG               | GTACTGCGAT<br>CATGACGCTA | AATTACAACA<br>TTAATGTTGT | ATGCTTAATG<br>TACGAATTAC | TGTCGGCAGA<br>ACAGCCGTCT | 701 |
| ATGGCTTCCA<br>TACCGAAGGT | GCCGTTTGTG<br>CGGCAAACAC | GGTTCATCAT<br>CCAAGTAGTA | TGGCGATTCA<br>ACCGCTAAGT | CTGATGCCGC               | 651 |
| CGACAAGGTG<br>GCTGTTCCAC | ATACGCAAGG<br>TATGCGTTCC | GGCAAATATT<br>CCGTTTATAA | TTTCACTATG<br>AAAGTGATAC | TCGCCCCCGT               | 601 |
| GACAACTTCT<br>CTGTTGAAGA | AGCCAATATG<br>TCGGTTATAC | ATTTAAACGT<br>TAAATTTGCA | ACCAGTTTTG<br>TGGTCAAAAC | GGTGAGTTTC<br>CCACTCAAAG | 551 |
| CCAATCCCTG<br>GGTTAGGGAC | TTCGTCTCAG<br>AAGCAGAGTC | GAATATGTTT<br>CTTATACAAA | GGTTTATTGA<br>CCAAATAACT | TTCCCTAAAG<br>AAGGGATTTC | 501 |
| CCTGGCCTAT<br>GGACCGGATA | ACGGTGAAAA<br>TGCCACTTTT | GTGGCGTGTT<br>CACCGCACAA | TTCGCAAGAT<br>AAGCGTTCTA | TACACATATA<br>ATGTGTATAT | 451 |
| CGGCAGTTTC<br>GCCGTCAAAG | CGACGATTTC<br>GCTGCTAAAG | GTGAATACCA<br>CACTTATGGT | TCGCTCTGGA               | AACGTTTTCA<br>TTGCAAAAGT | 401 |
| TCGTTTGACT               | CAAAAGGTAC               | AACAATGTGG               | CACAAGTGGG               | TATACCCTAT               |     |

## FIG. 34C

CGCCCCGCAT TAAAAAATT CCGTCAATAA CCCACGGGAA TTTGCGGACC

Bglii ~~~~~~ TGCTAGATCT TCC ACGATCTAGA AGG 801



| Н   | AATTCGAGCA<br>TTAAGCTCGT | GAAGCTGATC<br>CTTCGACTAG | TCTGAGGAGG<br>AGACTCCTCC | ATCTGTAGGG<br>TAGACATCCC | TGGTGGCTCT               |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 51  | GGTTCCGGTG               | ATTTTGATTA               | TGAAAAGATG               | GCAAACGCTA               | ATAAGGGGGC               |
|     | CCAAGGCCAC               | TAAAACTAAT               | ACTTTTCTAC               | CGTTTGCGAT               | TATTCCCCCG               |
| 101 | TATGACCGAA               | AATGCCGATG               | AAAACGCGCT               | ACAGTCTGAC               | GCTAAAGGCA               |
|     | ATACTGGCTT               | TTACGGCTAÇ               | TTTTGCGCGA               | TGTCAGACTG               | CGATTTCCGT               |
| 151 | AACTTGATTC               | TGTCGCTACT               | GATTACGGTG               | CTGCTATCGA               | TGGTTTCATT               |
|     | TTGAACTAAG               | ACAGCGATGA               | CTAATGCCAC               | GACGATAGCT               | ACCAAAGTAA               |
| 201 | GGTGACGTTT<br>CCACTGCAAA | CCGGCCTTGC               | TAATGGTAAT<br>ATTACCATTA | GGTGCTACTG<br>CCACGATGAC | GTGATTTTGC<br>CACTAAAACG |
| 251 | TGGCTCTAAT               | TCCCAAATGG               | CTCAAGTCGG               | TGACGGTGAT               | AATTCACCTT               |
|     | ACCGAGATTA               | AGGGTTTACC               | GAGTTCAGCC               | ACTGCCACTA               | TTAAGTGGAA               |
|     | ImmX                     | XmnI                     |                          |                          |                          |

EcoRI

FIG. 35B

CCCTCCCTCA ATCGGTTGAA GGGAGGGAGT TAGCCAACTT

TAATGAATAA TTTCCGTCAA TATTTACCTT ATTACTTATT AAAGGCAGTT ATAAATGGAA

301

| TTTCTATTGA<br>AAAGATAACT | CTTTTATATG<br>GAAAATATAC | ACTGCGTAAT<br>TGACGCATTA | CGCAGATTGT<br>GCGTCTAACA                      | S<br>O | 000000000000000000000000000000000000000 | GTTAAAATTC                    | CAATTTTAAG  |
|--------------------------|--------------------------|--------------------------|-----------------------------------------------|--------|-----------------------------------------|-------------------------------|-------------|
| CCATATGAAT<br>GGTATACTTA | CTTTGCGTTT<br>GAAACGCAAA | TTGCTAACAT<br>AACGATTGTA | TGAAAAATGG<br>ACTTTTTACC                      |        | AAGGGGGGGG                              | TTAATATTTT                    | AATTATAAAA  |
| CGCTGGTAAA<br>GCGACCATTT | TCCGTGGTGT<br>AGGCACCACA | TTTTCTACGT<br>AAAAGATGCA | ACCTGTGAAG<br>TGGACACTTC                      | PacI   | CGTTTAATTA<br>GCAAATTAAT                | ATTGTAAACG                    | TAACA'TTTGC |
| TTGTCTTTGG<br>AACAGAAACC | ATAAACTTAT<br>TATTTGAATA | TATGTATGTA<br>ATACATACAT | HindIII<br>~~~~~~<br>GATAAGCTTG<br>CTATTCGAAC |        | TTTTGTCTGC<br>AAAACAGACG                | BsrGi<br>~~~~~~<br>TGTACATGAA | ACATGTACTT  |
| TGTCGCCCTT<br>ACAGCGGGAA | TTGTGACAAA<br>AACACTGTTT | TTGCCACCTT<br>AACGGTGGAA | AAGGAGTCTT<br>TTCCTCAGAA                      | ·      | GCGACATTTT<br>CGCTGTAAAA                | TGGGGGGGGG                    | ACCCCCCCC   |
| 351                      | 401                      | 451                      | 501                                           |        | 551                                     | 601                           |             |

ACCCCCCCC ACATGRACT TAACATTTGC AATTATAAAA

FIG. 35C

|                          |                                           |                          | •                        |                          |                                   |                                     |
|--------------------------|-------------------------------------------|--------------------------|--------------------------|--------------------------|-----------------------------------|-------------------------------------|
| 9090990999               | AAAGGCCAGC<br>TTTCCGGTCG                  | TTTCCATAGG<br>AAAGGTATCC | GTCAGAGGTG<br>CAGTCTCCAC | CCTGGAAGCT<br>GGACCTTCGA | ATACCTGTCC<br>TATGGACAGG          | CACGCTGTAG<br>GTGCGACATC            |
| AACCACCACA<br>TTGGTGGTGT | CATGTGAGCA<br>GTACACTCGT                  | TGCTGGCGTT<br>ACGACCGCAA | CGACGCTCAA<br>GCTGCGAGTT | GGCGTTTCCC<br>CCGCAAAGGG | CGCTTACCGG                        | TCTCATAGCT<br>AGAGTATCGA            |
| CGCTGCGCGT<br>GCGACGCGCA | Nhel<br>~~~~~<br>GCGTGCTAGC<br>CGCACGATCG | AAGGCCGCGT<br>TTCCGGCGCA | TCACAAAAAT<br>AGTGTTTTTA | AAAGATACCA<br>TTTCTATGGT | CCGACCCTGC                        | CGTGGCGCTT<br>CGCCGCGAA<br>FIG. 35E |
| GTAGCGGTCA               | GCTACAGGGC<br>CGATGTCCCG                  | GAACCGTAAA<br>CTTGGCATTT | CTGACGAGCA<br>GACTGCCCGT | ACAGGACTAT<br>TGTCCTGATA | CTCTCCTGTT<br>GAGAGGACAA          | CTTCGGGAAG                          |
| GCTGGCAAGT               | TTAATGCGCC<br>AATTACGCGG                  | AAAAGGCCAG<br>TTTTCCGGTC | CTCCGCCCCC               | GCGAAACCCG<br>CGCTTTGGGC | BSSSI<br>CCCTCGTGCG<br>GGGAGCACGC | GCCTTTCTCC<br>CGGAAAGAGG            |
| 1001                     | 1051                                      | 1101                     | 1151                     | 1201                     | 1251                              | 1301                                |

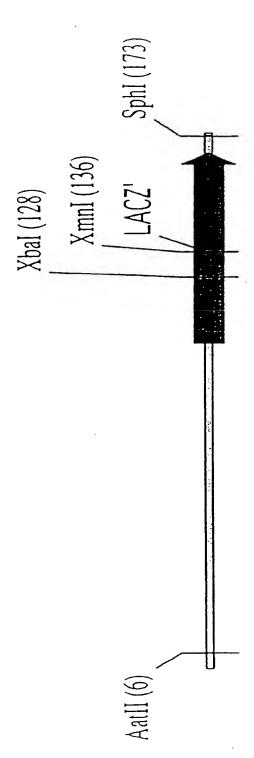
| TGTGTGCACG | CTATCGTCTT | CAGCCACTGG | GAGTTCTTGA | TGGTATCTGC | GCTCTTGATC | TGCAAGCAGC | GATCTTTTCT |
|------------|------------|------------|------------|------------|------------|------------|------------|
| ACACACGTGC | GATAGCAGAA | GTCGGTGACC | CTCAAGAACT | ACCATAGACG | CGAGAACTAG | ACGTTCGTCG | CTAGAAAAGA |
| CAAGCTGGGC | TATCCGGTAA | CCACTGGCAG | CGGTGCTACA | GAACAGTATT | AGAGTTGGTA | TTTTTTTGTT | AAGATCCTTT |
| GTTCGACCCG | ATAGGCCATT | GGTGACCGTC | GCCACGATGT | CTTGTCATAA | TCTCAACCAT | AAAAAAACAA | TTCTAGGAAA |
| TCGTTCGCTC | CGCTGCGCCT | CGACTTATCG | GGTATGTAGG | TACACTAGAA | CTTCGGAAAA | GTAGCGGTGG | GGATCTCAAG |
| AGCAAGCGAG |            | GCTGAATAGC | CCATACATCC | ATGTGATCTT | GAAGCCTTTT | CATCGCCACC | CCTAGAGTTC |
| TCGGTGTAGG | TCAGCCCGAC | CGGTAAGACA | AGCAGAGCGA | TAACTACGGC | AGCCAGTTAC | ACCACCGCTG | CAGAAAAAA  |
| AGCCACATCC |            | GCCATTCTGT | TCGTCTCGCT | ATTGATGCCG | TCGGTCAATG | TGGTGGCGAC | GTCTTTTTTT |
| GTATCTCAGT | AACCCCCCGT | GAGTCCAACC | TAACAGGATT | AGTGGTGGCC | GCTCTGCTGT | CGGCAAACAA | AGATTACGCG |
| CATAGAGTCA | TTGGGGGGCA | CTCAGGTTGG | ATTGTCCTAA | TCACCACCGG | CGAGACGACA | GCCGTTTGTT | TCTAATGCGC |
| 1351       | 1401       | 1451       | 1501       | 1551       | 1601       | 1651       | 1701       |

FIG. 35F

| GGATTTTGGT               | TTAAAAAAAT                                 | CATTAAGCAT | TGAATCGCCA               | CATAGTGAAA               | CAAAACTGGT               | TCAATAAACC               |
|--------------------------|--------------------------------------------|------------|--------------------------|--------------------------|--------------------------|--------------------------|
| CCTAAAACCA               | AATTTTTTA                                  | GTAATTCGTA | ACTTAGCGGT               | GTATCACTTT               | GTTTTGACCA               | AGTTATTTGG               |
| TCACGTTAAG               | AATAACTGCC                                 | TGTTGTAATT | ATGATGAACC               | AATATTTGCC               | ACGTTTAAAT               | AAACATATTC               |
| AGTGCAATTC               | TTATTGACGG                                 | ACAACATTAA | TACTACTTGG               | TTATAAACGG               | TGCAAATTTA               | TTTGTATAAG               |
| GAACGAAAAC               | TAAGGGCACC                                 | ATCGCAGTAC | CACAAACGGC               | CCTTGCGTAT               | CATATTGGCT               | CTGAGACGAA               |
| CTTGCTTTTG               | ATTCCCGTGG                                 | TAGCGTCATG | GTGTTTGCCG               | GGAACGCATA               | GTATAACCGA               | GACTCTGCTT               |
| ACGCTCAGTG               | ACCAGGCGTT                                 | CCTGCCACTC | TGGAAGCCAT               | CACCTTGTCG               | AGAAGTTGTC               | CAGGGATTGG               |
| TGCGAGTCAC               | TGGTCCGCAA                                 | GGACGGTGAG | ACCTTCGGTA               | GTGGAACAGC               | TCTTCAACAG               | GTCCCTAACC               |
| ACGGGGTCTG<br>TGCCCCAGAC | Bglii<br>~~~~~<br>CAGATCTAGC<br>GTCTAGATCG | TACGCCCCGC | TCTGCCGACA<br>AGACGGCTGT | GCGGCATCAG<br>CGCCGTAGTC | ACGGGGGCGA<br>TGCCCCCGCT | GAAACTCACC<br>CTTTGAGTGG |
| 1751                     | 1801                                       | 1851       | 1901                     | 1951                     | 2001                     | 2051                     |

| 2101 | CTTTAGGGAA | ATAGGCCAGG | TTTTCACCGT | AACACGCCAC | ATCTTGCGAA |
|------|------------|------------|------------|------------|------------|
|      | GAAATCCCTT | TATCCGUTCC | AAAAGTGGCA | TTGTGCGGTG | TAGAACGCTT |
| 2151 | TATATGTGTA | GAAACTGCCG | GAAATCGTCG | TGGTATTCAC | TCCAGAGCGA |
|      | ATATACACAT | CTTTGACGGC | CTTTAGCAGC | ACCATAAGTG | AGGTCTCGCT |
| 2201 | TGAAAACGTT | TCAGTTTGCT | CATGGAAAAC | GGTGTAACAA | GGGTGAACAC |
|      | ACTTTTGCAA | AGTCAAACGA | GTACCTTTTG | CCACATTGTT | CCCACTTGTG |
| 2251 | TATCCCATAT | CACCAGCTCA | CCGTCTTTCA | TTGCCATACG | GAACTCCGGG |
|      | ATAGGGTATA | GTGGTCGAGT | GGCAGAAAGT | AACGGTATGC | CTTGAGGCCC |
| 2301 | TGAGCATTCA | TCAGGCGGGC | AAGAATGTGA | ATAAAGGCCG | GATAAAACTT |
|      | ACTCGTAAGT | AGTCCGCCCG | TTCTTACACT | TATTTCCGGC | CTATTTTGAA |
| 2351 | GTGCTTATTT | TTCTTTACGG | TCTTTAAAAA | GGCCGTAATA | TCCAGCTGAA |
|      | CACGAATAAA | AAGAAATGCC | AGAAATTTTT | CCGGCATTAT | AGGTCGACTT |
| 2401 | CGGTCTGGTT | ATAGGTACAT | TGAGCAACTG | ACTGAAATGC | CTCAAAATGT |
|      | GCCAGACCAA | TATCCATGTA | ACTCGTTGAC | TGACTTTACG | GAGTTTTACA |
| 2451 | TCTTTACGAT | GCCATTGGGA | TATATCAACG | GTGGTATATC | CAGTGATTTT |
|      | AGAAATGCTA | CGGTAACCCT | ATATAGTTGC | CACCATATAG | GTCACTAAAA |

|                                                                                            | 99999                                           | 2751 |
|--------------------------------------------------------------------------------------------|-------------------------------------------------|------|
|                                                                                            | EcoRI                                           |      |
| GAG<br>CTC                                                                                 | TTCACACAGG A<br>AAGTGTGTCC T                    | 2701 |
| Xbal Sphi                                                                                  |                                                 |      |
| CCGGCTCGTA TGTTGTGTGG AATTGTGAGC GGATAACAAT<br>GGCCGAGCAT ACAACACACC TTAACACTCG CCTATTGTTA | CTTTATGCTT C<br>GAAATACGAA G                    | 2651 |
| ATGTGAGTTA GCTCACTCAT TAGGCACCCC AGGCTTTACA<br>TACACTCAAȚ CGAGTGAGTA ATCCGTGGGG TCCGAAATGT | Aatii<br>~~~~~~<br>CCGACGTCTA A<br>GGCTGCAGAT T | 2601 |
| TAGTGATCTT ATTTCATTAT GGTGAAAGTT GGAACCTCAC<br>ATCACTAGAA TAAAGTAATA CCACTTTCAA CCTTGGAGTG | ATACGCCCGG T<br>TATGCGGGCC A                    | 2551 |
| TTAGCTTCCT TAGCTCCTGA AAATCTCGAT AACTCAAAAAAAAAA                                           | TTTCTCCATT T<br>AAAGAGGTAA A                    | 2501 |



M2 173 bp **F/G. 35J** 

AatII

111111

CTCACTCATT AGGCACCCCA GGCTTTACAC CCGAAATGTG TCCGTGGGGT GAGTGAGTAA ACACTCAATC TGTGAGTTAG GACGTCTTAA CTGCAGAATT

CTATTGTTAA GATAACAATT GTTGTGTGA ATTGTGAGCG TAACACTCGC CAACACACCT CGGCTCGTAT GCCGAGCATA AAATACGAAG TTTATGCTTC 2

XmnI

XbaI

111111

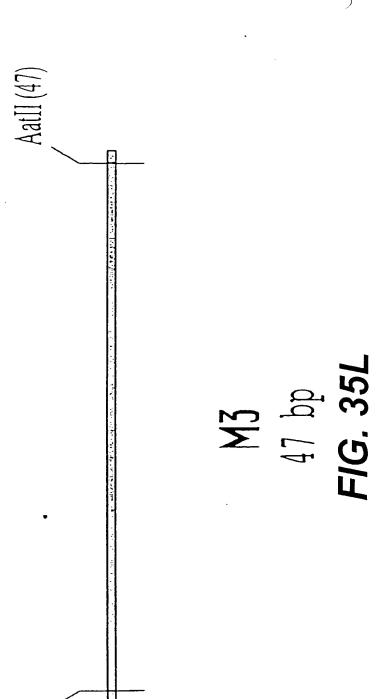
CATATTACAT GTATAATGTA TCACACAGGA AACAGCTATG ACCATGTCTA GAATAACTTC TGGTACAGAT CTTATTGAAG TTGTCGATAC AGTGTGTCCT

101

SphI

TCAATAGCGT ACG CGCTATACGA AGTTATCGCA GCGATATGCT 151

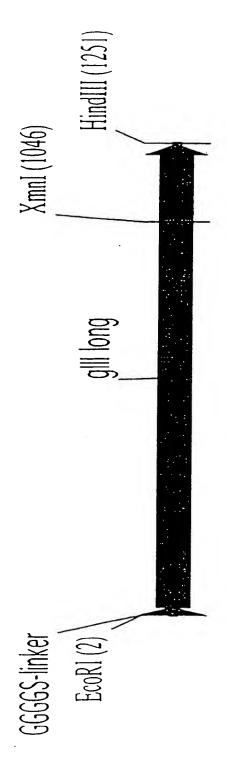
FIG. 35K



AatlI

TGACGTC ACTGCAG AGATCTCATA ACTTCGTATA ATGTATGCTA TACGAAGTTA TCTAGAGTAT TGAAGCATAT TACATACGAT ATGCTTCAAT

 $\mathbf{\Sigma}$ 



M7-I (long) 1255 bp *FIG.* 35N

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ECORI

|        | 1 1 1 1 1 1              | -                        |                          |                          |                          |
|--------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
|        | GAATTCGGTG<br>CTTAAGCCAC | GTGGTGGATC<br>CACCACCTAG | TGCGTGCGCT<br>ACGCACGCGA | GAAACGGTTG<br>CTTTGCCAAC | AAAGTTGTTT<br>TTTCAACAAA |
| 51     | AGCAAAATCC               | CATACAGAAA               | ATTCATTTAC               | TAACGTCTGG               | AAAGACGACA               |
| 101    |                          | 正している 日本でした              |                          |                          |                          |
| H<br>D | TTTGAAATCT               | AGCAATGCGA               | TTGATACTCC               | CGACAGACAC               | CTTACGATGT               |
| 151    | GGCGTTGTAG               | TTTGTACTGG               | TGACGAAACT               | CAGTGTTACG               | GTACATGGGT               |
|        | CCGCAACATC               | AAACATGACC               | ACTGCTTTGA               | GTCACAATGC               | CATGTACCCA               |
| 201    | TCCTATTGGG               | CITGCIAICC               | CTGAAAATGA               | GGGTGGTGGC               | TCTGAGGGTG               |
|        | AGGATAACCC               | GAACGATAGG               | GACTTTTACT               | CCCACCACCG               | AGACTCCCAC               |
| 251    | GCGGTTCTGA               | GGGTGGCGGT               | TCTGAGGGTG               | GCGGTACTAA               | ACCTCCTGAG               |
|        | コンピラムマンンラン               |                          | フザンフン・フザウザ               | CGCCAIGAIL               | Tocaccaci                |

FIG. 350

CACCTATTCC GGGCTATACT TATATCAACC CTCTCGACGG GTGGATAAGG CCCGATATGA ATATAGTTGG GAGAGCTGCC

TACGGTGATA ATGCCACTAT

301

| 351 | CACTTATCCG               | CCTGGTACTG               | AGCAAAACCC               | CGCTAATCCT               | AATCCTTCTC               |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
|     | GTGAATAGGC               | GGACCATGAC               | TCGTTTTGGG               | GCGATTAGGA               | TTAGGAAGAG               |
| 401 | TTGAGGAGTC               | TCAGCCTCTT               | AATACTTTCA               | TGTTTCAGAA               | TAATAGGTTC               |
|     | AACTCCTCAG               | AGTCGGAGAA               | TTATGAAAGT               | ACAAAGTCTT               | ATTATCCAAG               |
| 451 | CGAAATAGGC               | AGGGGGCATT               | AACTGTTTAT               | ACGGGCACTG               | TTACTCAAGG               |
|     | GCTTTATCCG               | TCCCCCGTAA               | TTGACAAATA               | TGCCCGTGAC               | AATGAGTTCC               |
| 501 | CACTGACCCC               | GTTAAAACTT               | ATTACCAGTA               | CACTCCTGTA               | TCATCAAAAG               |
|     | GTGACTGGGG               | CAATTTTGAA               | TAATGGTCAT               | GTGAGGACAT               | AGTAGTTTTC               |
| 551 | CCATGTATGA               | CGCTTACTGG               | AACGGTAAAT               | TCAGAGACTG               | CGCTTTCCAT               |
|     | GGTACATACT               | GCGAATGACC               | TTGCCATTTA               | AGTCTCTGAC               | GCGAAAGGTA               |
| 601 | TCTGGCTTTA               | ATGAGGA TTT              | ATTTGTTTGT               | GAATATCAAG               | GCCAATCGTC               |
|     | AGACCGAAAT               | TACTCCTAAA               | TAAACAAACA               | CTTATAGTTC               | CGGTTAGCAG               |
| 651 | TGACCTGCCT<br>ACTGGACGGA | CAACCTCCTG               | TCAATGCTGG<br>AGTTACGACC | CGGCGGCTCT               | GGTGGTGGTT<br>CCACCACCAA |
| 701 | CTGGTGGCGG<br>GACCACCGCC | CTCTGAGGGT<br>GAGACTCCCA | GGTGGCTCTG               | AGGGTGGCGG<br>TCCCACCGCC | TTCTGAGGGT<br>AAGACTCCCA |

FIG. 35P

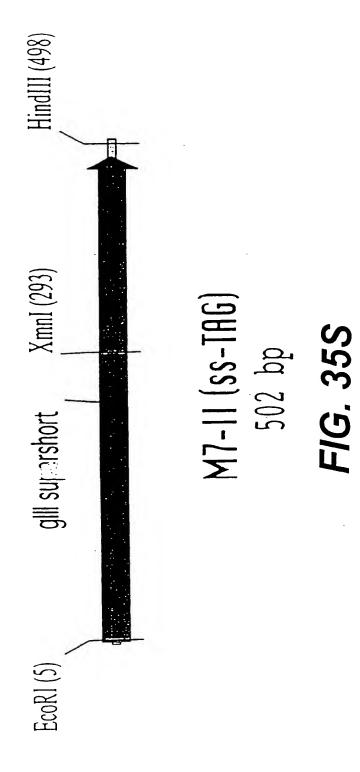
| GCCCTTTTGT |            | CCCTCAATCG | TACCTTCCAT | CGTCAATATT | 1051 |
|------------|------------|------------|------------|------------|------|
| GAATAATTTC | CACCTTTAAT | GGTGATAATT | AGTCGGTGAA | AAATGGCTCA | 1001 |
| CTTATTAAAG | GTGGAAATTA | CCACTATTAA | TCAGCCACTT | TTTACCGAGT |      |
|            |            |            | ·          |            |      |
| TCTAATTCCC | TTTTGCTGGC | CTACTGGTGA | GGTAATGGTG | CCTTGCTAAT | 951  |
| AGATTAAGGG | AAAACGACCG | GATGACCACT | CCATTACCAC | GGAACGATTA |      |
| ACGTTTCCGG | TTCATTGGTG | TATCGATGGT | ACGGTGCTGC | GCTACTGATT | 901  |
| TGCAAAGGCC | AAGTAACCAC | ATAGCTACCA | TGCCACGACG | CGATGACTAA |      |
| TGATTCTGTC | AAGGCAAACT | TCTGACGCTA | CGCGCTACAG | CCGATGAAAA | 851  |
| ACTAAGACAG | TTCCGTTTGA | AGACTGCGAT | GCGCGATGTC | GGCTACTTTT |      |
| ACCGAAAATG | GGGGGCTATG | ACGCTAATAA | AAGATGGCAA | TGATTATGAA | 801  |
| TGGCTTTTAC | CCCCCGATAC | TGCGATTATT | TTCTACCGTT | ACTAATACTT |      |
| CCGGTGATTT | GGCTCTGGTT | TTCCGGTGGT | AGGGAGGCGG | GGCGGCTCTG | 751  |
| GGCCACTAAA | CCGAGACCAA | AAGGCCACCA | TCCCTCCGCC | CCGCCGAGAC |      |

GCAGTTATAA ATGGAAGGTA GGGAGTTAGC CAACTTACAG CGGGAAAACA

FIG. 35Q

|                          |                                                                                                                 |                          |                          | AGCTT                    | 1251 |
|--------------------------|-----------------------------------------------------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|------|
|                          |                                                                                                                 |                          |                          | <i>t t t t</i>           |      |
|                          |                                                                                                                 |                          |                          | HindI                    |      |
| AGTCTTGATA<br>TCAGAACTAT | CGTAATAAGG                                                                                                      | TAACATACTG<br>ATTGTATGAC | CTACGTTEGC<br>GATGCAAACG | TATGTATTTT<br>ATACATAAAA | 1201 |
| HindIII                  |                                                                                                                 |                          |                          |                          |      |
| CACCTTTATG<br>GTGGAAATAC | TATATGTTGC<br>ATATACAACG                                                                                        | GCGTTTCTTT<br>CGCAAAGAAA | TGGTGTCTTT<br>ACCACAGAAA | ACTTATTCCG<br>TGAATAAGGC | 1151 |
| GACAAAATAA<br>CTGTTTTATT | CTTTGGCGCT GGTAAACCCT ATGAATTTTC TATTGATTGT GACAAATAA<br>GAAACCGCGA CCATTTGGGA TACTTAAAAG ATAACTAACA CTGTTTTATT | ATGAATTTTC<br>TACTTAAAAG | GGTAAACCCT<br>CCATTTGGGA | CTTTGGCGCT               | 1101 |

F/G. 35R



# M 7-II (SS-TAG):

# ECORI

| GTGATTTTGA                       | CACTAAAACT            |
|----------------------------------|-----------------------|
| CGGTGGTGGC TCTGGTTCCG GTGATTTTGA | GCCACCACCG AGACCAAGGC |
| CGGTGGTGGC                       | GCCACCACCG            |
| GAGGCGGTTC                       | CTCCGCCAAG            |
| CGGGAATTCG                       | GCCCTTAAGC            |
| -                                |                       |

| GAAAATGCCG                                      | CTTTTACGGC       |
|-------------------------------------------------|------------------|
| AAG ATGGCAAACG CTAATAAGGG GGCTATGACC GAAAATGCCG | PACTEG           |
| CTAATAAGGG                                      | GATTATTCCC CCGA1 |
| ATGGCAAACG                                      | TACCGTTTGC       |
| TTATGAAAAG                                      | AATACTTTTC TA    |
| 51                                              |                  |

| AAAACGC GCTACAGTCT GACGCTAAAG GCAAACTTGA TTCTGTCGCT | TIGGG CGAIGICAGA CIGCGAITIC CGIIIGAACI AAGACAGCGA |
|-----------------------------------------------------|---------------------------------------------------|
| GCAAACTTGA                                          | CGTTTGAACT                                        |
| GACGCTAAAG                                          | CTGCGATTTC                                        |
| GCTACAGTCT                                          | PTGCG CGATGTCAGA                                  |
| ATGAAAACGC                                          | TACTTTTGCG                                        |
| 101                                                 |                                                   |

### XmnI

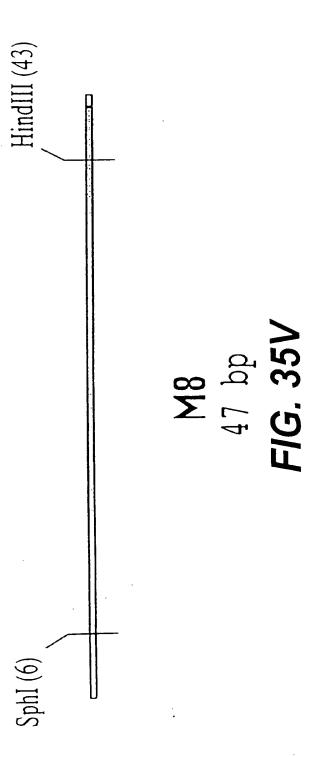
ATTAAAGGCA TAATTTCCGT CTTTAATGAA GAAATTACTT CGGTGACGGT GATAATTCAC GCCACTGCCA CTATTAAGTG TGGCTCAAGT ACCGAGTTCA 251

## FIG. 35T

|                                         |                                                |                          |                          | Hi<br>~                  |     |
|-----------------------------------------|------------------------------------------------|--------------------------|--------------------------|--------------------------|-----|
| HindIII<br><br>CTTGATAAGC<br>GAACTATTCG | AATAAGGAGT<br>TTATTCCTCA                       | CATACTGCGT<br>GTATGACGCA | CGTTTGCTAA<br>GCAAACGATT | GTATTTTTA                | 451 |
| CTTTATGTAT<br>GAAATACATA                | ATGTTGCCAC<br>TACAACGGTG                       | TTTCTTTAT<br>AAAGAAAATA  | TGTCTTTGCG<br>ACAGAAACGC | TATTCCGTGG<br>ATAAGGCACC | 401 |
| AAAATAAACT<br>TTTTATTTGA                | TGATTGTGAC<br>ACTAACACTG                       | AATTTTCTAT<br>TTAAAAGATA | AAACCATATG<br>TTTGGTATAC | TGGCGCTGGT               | 351 |
| CTTTGTCTT<br>GAAAACAGAA                 | GAATGTCGCC CTTTTGTCTT<br>CTTACAGCGG GAAAACAGAA | TCAATCGGTT<br>AGTTAGCCAA | CTTCCCTCCC               | CAATATTTAC<br>GTTATAAATG | 301 |

TT

501

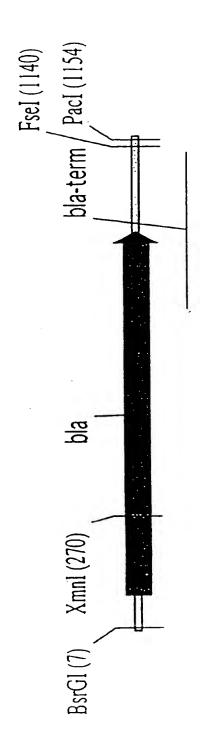


HindIII

GCATGCCATA ACTTCGTATA ATGTACGCTA TACGAAGTTA TAAGCTT CGTACGGTAT TGAAGCATAT TACATGCGAT ATGCTTCAAT ATTCGAA

FIG. 35W

.. დ Σ SphI



M10-II 1163 bp *FIG.* 35X

## BsrGI

| AACCCTGATA               | CAACATTTCC               | TGTTTTTGCT | AGTTGGGTGC               | ATCCTTGAGA               |
|--------------------------|--------------------------|------------|--------------------------|--------------------------|
| TTGGGACTAT               | GTTGTAAAGG               | ACAAAAACGA | TCAACCCACG               | TAGGAACTCT               |
| ATGAGACAAT<br>TACTCTGTTA | TATGAGTATT<br>ATACTCATAA | TTTGCCTTCC | GCTGAGGATC               | CAGCGGTAAG<br>GTCGCCATTC |
| GTATCCGCTC               | AAAGGAAGAG               | TTTGCGGCAT | AGTAAAAGAT               | TGGATCTCAA               |
| CATAGGCGAG               | TTTCCTTCTC               | AAACGCCGTA | TCATTTTCTA               | ACCTAGAGTT               |
| ATTCAAATAT               | TAATATTGAA               | TATTCCCTTT | CGCTGGTGAA               | TACATCGAAC               |
| TAAGTTTATA               | ATTATAACTT               | ATAAGGGAAA | GCGACCACTT               | ATGTAGCTTG               |
| GGGGGTGTAC               | AATGCTTCAA<br>TTACGAAGTT | GTGTCGCCCT | CACCCAGAAA<br>GTGGGTCTTT | GCGAGTGGGT<br>CGCTCACCCA |
| Н                        | 51                       | 101        | 151                      | 201                      |

## FIG. 35Y

GTTTTCGCCC CGAAGAACGT TTTCCAATGA TGAGCACTTT TAAAGTTCTG CAAAAGCGGG GCTTCTTGCA AAAGGTTACT ACTCGTGAAA ATTTCAAGAC

251

XmnI

| 301 | CTATGTGGCG<br>GATACACCGC | CGGTATTATC<br>GCCATAATAG | CCGTATTGAC<br>GGCATAACTG | GCCGGGCAAG               | AGCAACTCGG<br>TCGTTGAGCC |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 351 | TCGCCGCATA<br>AGCGGCGTAT | CACTATTCTC<br>GTGATAAGAG | AGAATGACTT<br>TCTTACTGAA | GGTTGAGTAC               | TCACCAGTCA<br>AGTGGTCAGT |
| 401 | CAGAAAAGCA<br>GTCTTTTCGT | TCTTACGGAT<br>AGAATGCCTA | GGCATGACAG<br>CCGTACTGTC | TAAGAGAATT<br>ATTCTCTTAA | ATGCAGTGCT               |
| 451 | GCCATAACCA<br>CGGTATTGGT | TGAGTGATAA<br>ACTCACTATT | CACTGCGGCC<br>GTGACGCCGG | AACTTACTTC<br>TTGAATGAAG | TGACAACGAT<br>ACTGTTGCTA |
| 501 | CGGAGGACCG               | AAGGAGCTAA<br>TTCCTCGATT | CCGCTTTTTT<br>GGCGAAAAAA | GCACAACATG<br>CGTGTTGTAC | GGGGATCATG<br>CCCCTAGTAC |
| 551 | TAACTCGCCT<br>ATTGAGCGGA | TGATCGTTGG<br>ACTAGCAACC | GAACCGGAGC<br>CTTGGCCTCG | TGAATGAAGC<br>ACTTACTTCG | CATACCAAAC<br>GTATGGTTTG |
| 601 | GACGAGCGTG               | ACACCACGAT<br>TGTGGTGCTA | GCCTGTAGCA               | ATGCCAACAA               | CGTTGCGCAA<br>GCAACGCGTT |
| 651 | ACTATTAACT<br>TGATAATTGA | GGCGAACTAC<br>CCGCTTGATG | TTACTCTAGC<br>AATGAGATCG | TTCCCGGCAA<br>AAGGGCCGTT | CAGTTAATAG<br>GTCAATTATC |

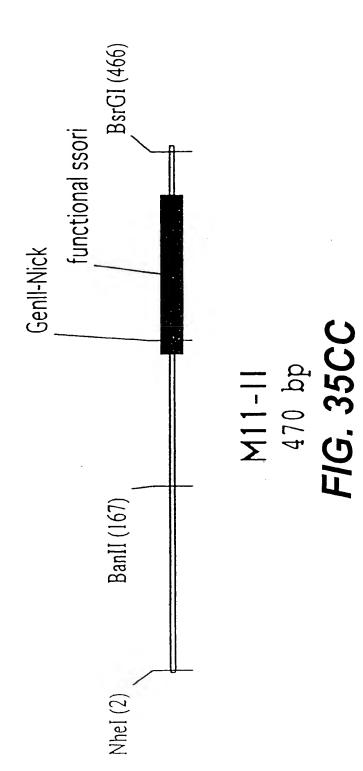
FIG. 35Z

| CTCGGCCCTT               | AGCGTGGGTC | TCCCGTATCG  | ACGAAATAGA               | TAACTGTCAG               | TCATTTTAA                | TGACCAAAAT               | GTAGAAAAGA               |
|--------------------------|------------|-------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| GAGCCGGGAA               | TCGCACCCAG | AGGGCATAGC  | TGCTTTATCT               | ATTGACAGTC               | AGTAAAAATT               | ACTGGTTTTA               | CATCTTTTCT               |
| CACTTCTGCG               | GGAGCCGGTG | TGGTAAGCCC  | CTATGGATGA               | AAGCATTGGG               | ATTTAAAACT               | GATAATCTCA               | GTCAGACCCC               |
| GTGAAGACGC               | CCTCGGCCAC | ACCATTCGGG  | GATACCTACT               | TTCGTAACCC               | TAAATTTTGA               | CTATTAGAGT               | CAGTCTGGGG               |
| GTTGCAGGAC               | TGATAAATCT | TGGGGCCAGA  | AGTCAGGCAA               | CTCACTGATT               | CTTTAGATTG               | GATCCTTTTT               | TCCACTGAGC               |
|                          | ACTATTTAGA | ACCCCGGTCT  | TCAGTCCGTT               | GAGTGACTAA               | GAAATCTAAC               | CTAGGAAAAA               | AGGTGACTCG               |
| GGCGGATAAA               | GGTTTATTGC | ATTGCAGCAC  | CACGACGGGG               | AGATAGGTGC               | CTCATATATA               | TCTAGGTGAA               | GAGTTTTCGT               |
| CCGCCTATTT               | CCAAATAACG | TAACGTCGTG  | GTGCTGCCCC               | TCTATCCACG               | GAGTATATAT               | AGATCCACTT               | CTCAAAAGCA               |
| ACTGGATGGA<br>TGACCTACCT | CCGGCTGGCT | TCGCGGGTATC | TAGTTATCTA<br>ATCAATAGAT | CAGATCGCTG<br>GTCTAGCGAC | ACCAAGTTTA<br>TGGTTCAAAT | TTTAAAAGGA<br>AAATTTTCCT | CCCTTAACGT<br>GGGAATTGCA |
| 701                      | 751        | 801         | 851                      | 901                      | 951                      | 1001                     | 1051                     |

# FIG. 35AA

| PacI | 1                                       | CCCCCCCTT                |
|------|-----------------------------------------|--------------------------|
| FseI | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | AATGGCCGGC<br>TTACCGGCCG |
|      |                                         | CCTTTTTGAT<br>GGAAAAACTA |
|      |                                         | TTCTTGAGAT<br>AAGAACTCTA |
|      |                                         | TCAAAGGATC<br>AGTTTCCTAG |
|      |                                         | 1101                     |

PacI



## M11-II:

NheI

| GTGGGCCATC               | GGTTCTCGTA<br>CCAAGAGCAT               | TTAGGGTGAT<br>AATCCCACTA | AAAAACTTGA<br>TTTTTGAACT                   | CTCGACCCCA<br>GAGCTGGGGT | 201      |
|--------------------------|----------------------------------------|--------------------------|--------------------------------------------|--------------------------|----------|
| TTTACGGCAC<br>AAATGCCGTG | GATTTAGTGC<br>CTAAATCACG               | TTAGGGTTCC               | BanII<br>~~~~~<br>GGGGCTCCCT<br>CCCCGAGGGA | CTCTAAATCG<br>GAGATTTAGC | 151      |
| GGGCAGTTC                | GCGGCCGAAA                             | AGCGGTGCAA               | GGAAGGAAAG                                 | GCGAAAGAAG               |          |
| CCGCTCCTTT<br>GGCGAGGAAA | GCCCTAGCGC<br>CGGGATCGCG               | ACTTGCCAGC<br>TGAACGGTCG | TGACCGCTAC<br>ACTGGCGATG                   | ACGCGCAGCG<br>TGCGCGTCGC | 5        |
| TGTGGTGGTT<br>ACACCACCAA | )<br> <br>   <br>   <br>   <br>   <br> | GGCGCATTAA<br>CCGCGTAATT | GCCCTGTAGC<br>CGGGACATCG                   | GCTAGCACGC<br>CGATCGTGCG | <b>~</b> |

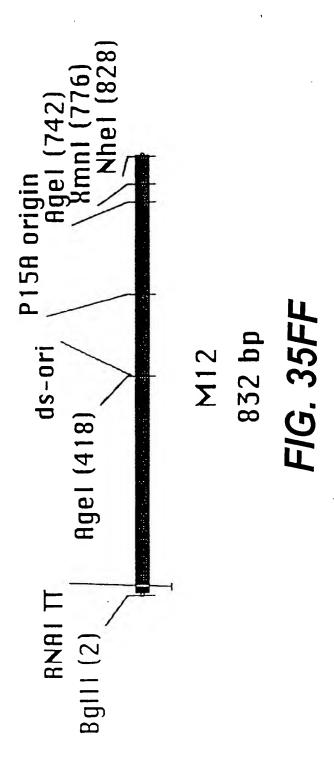
# FIG. 35DD

GCCCTGATAG ACGGTTTTTC GCCCTTTGAC GTTGGAGTCC ACGTTCTTTA CGGGAAACTG CAACCTCAGG TGCAAAAAT

251

|                          |                                                                                                                  |                          | BSrGI<br>CGTTTACAAT TTCATGTACA<br>GCAAATGTTA AAGTACATGT | CGTTTACAAT<br>GCAAATGTTA | 451 |
|--------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------|---------------------------------------------------------|--------------------------|-----|
| AAAATATTAA<br>TTTTATAATT | AAATGAGCTG ATTTAACAAA AATTTAACGC GAATTTTAAC AAAATATTAA<br>TTTACTCGAC TAAATTGTTT TTAAATTGCG CTTAAAATTG TTTTATAATT | AATTTAACGC<br>TTAAATTGCG | ATTTAACAAA<br>TAAATTGTTT                                | AAATGAGCTG<br>TTTACTCGAC | 401 |
| ATTGGTTAAA<br>TAACCAATTT | TATTCTTTTG ATTTATAAGG GATTTTGCCG ATTTCGGCCT ATTGGTTAAA<br>ATAAGAAAAC TAAATATTCC CTAAAACGGC TAAAGCCGGA TAACCAATTT | GATTTTGCCG<br>CTAAAACGGC | TATTCTTTTG ATTTATAAGG<br>ATAAGAAAAC TAAATATTCC          | TATTCTTTTG<br>ATAAGAAAAC | 351 |
| TATCTCGGTC<br>ATAGAGCCAG | ATAGTGGACT CTTGTTCCAA ACTGGAACAA CACTCAACCC TATCTCGGTC<br>TATCACCTGA GAACAAGGTT TGACCTTGTT GTGAGTTGGG ATAGAGCCAG | ACTGGAACAA<br>TGACCTTGTT | ATAGTGGACT CTTGTTCCAA<br>TATCACCTGA GAACAAGGTT          | ATAGTGGACT<br>TATCACCTGA | 301 |

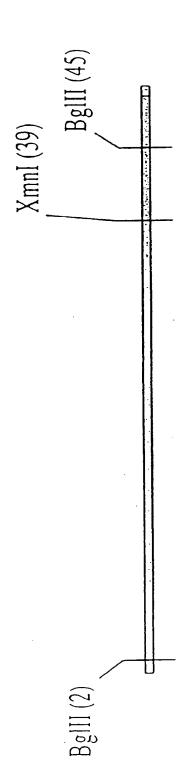
FIG. 35EE



| ~   | ~~~~~~<br>AGATCTAATA<br>TCTAGATTAT | AGATGATCTT<br>TCTACTAGAA | CTTGAGATCG<br>GAACTCTAGC | TTTTGGTCTG               | CGCGTAATCT<br>GCGCATTAGA |
|-----|------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 51  | CTTGCTCTGA<br>GAACGAGACT           | AAACGAAAAA<br>TTTGCTTTTT | ACCGCCTTGC<br>TGGCGGAACG | AGGGCGGTTT<br>TCCCGCCAAA | TTCGTAGGTT<br>AAGCATCCAA |
| 101 | CTCTGAGCTA<br>GAGACTCGAT           | CCAACTCTTT<br>GGTTGAGAAA | GAACCGAGGT<br>CTTGGCTCCA | AACTGGCTTG<br>TTGACCGAAC | GAGGAGCGCA<br>CTCCTCGCGT |
| 151 | GTCACTAAAA<br>CAGTGATTTT           | CTTGTCCTTT<br>GAACAGGAAA | CAGTTTAGCC<br>GTCAAATCGG | TTAACCGGCG<br>AATTGGCCGC | CATGACTTCA<br>GTACTGAAGT |
| 201 | AGACTAACTC<br>TCTGATTGAG           | CTCTAAATCA<br>GAGATTTAGT | ATTACCAGTG<br>TAATGGTCAC | GCTGCTGCCA               | GTGGTGCTTT<br>CACCACGAAA |
| 251 | TGCATGTCTT<br>ACGTACAGAA           | TCCGGGTTGG               | ACTCAAGACG<br>TGAGTTCTGC | ATAGTTACCG<br>TATCAATGGC | GATAAGGCGC<br>CTATTCCGCG |
| 301 | AGCGGTCGGA<br>TCGCCAGCCT           | CTGAACGGGG<br>GACTTGCCCC | GGTTCGTGCA<br>CCAAGCACGT | TACAGTCCAG<br>ATGTCAGGTC | CTTGGAGCGA               |

FIG. 35GG

| 701    | <b>するいじしじするい</b> り | ТАТАТОПОПОТ                      | COCASHOSHO THATACAOTA TATATATATA AACSOBAASS |            | AG@L<br>111111111111111111111111111111111111 |
|--------|--------------------|----------------------------------|---------------------------------------------|------------|----------------------------------------------|
| H<br>> | CCTTCGCCTT         | ATATAGGACA                       | TAGTGTATAA                                  |            | TGGCCACGTC                                   |
|        |                    |                                  | Xmn I                                       |            |                                              |
| 751    | CCTTTTTTCT         | CCTTTTTTCT CCTGCCACAT GAAGCACTTC | GAAGCACTTC                                  | ACTGACACCC | TCATCAGTGC                                   |
|        | GGAAAAAAGA         | GGAAAAAGA GGACGGTGTA             | CTTCGTGAAG                                  | TGACTGTGGG | AGTAGTCACG                                   |
|        |                    |                                  | NheI                                        |            |                                              |
| 801    | CAACATAGTA         | AGCCAGTATA                       | CAACATAGTA AGCCAGTATA CACTCCGCTA GC         | ပ္ပ        |                                              |
|        | GTTGTATCAT         | TCGGTCATAT                       | GTGAGGCGAT                                  | 90         |                                              |
|        |                    |                                  | (                                           |            |                                              |



M13 49 bp *FIG. 35JJ* 

M 13:

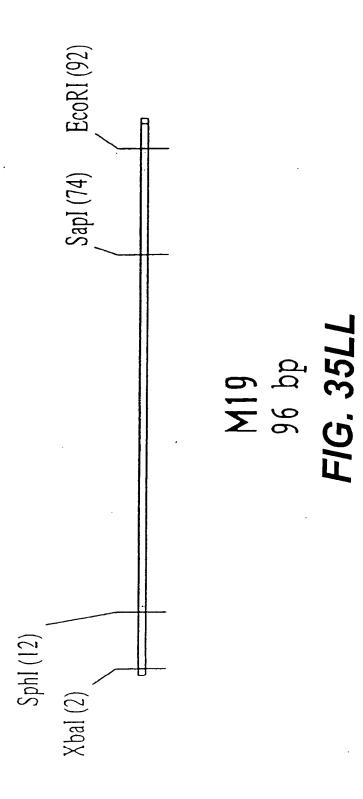
BglII

AGATCTCATA ACTTCGTATA ATGTATGCTA TACGAAGTTA TTCAGATCT TCTAGAGTAT TGAAGCATAT TACATACGAT ATGCTTCAAT AAGTCTAGA

BglII

XmnI

## FIG. 35KK



ECORI

M 19

XbaI SphI

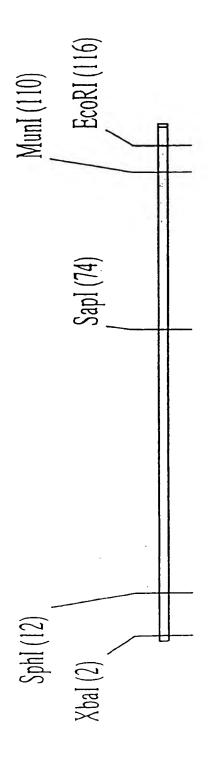
CTATTGCACT AAACAAAGCA TTTGTTTCGT AAATAAAATG TTTATTTAC GCGTAGGAGA AGATCTCGTA TCTAGAGCAT

Sapi

TACCAAAGCC ATGGTTTCGG CCGTTGCTCT TCACCCCTGT GGCAACGAGA AGTGGGGACA GGCACTCTTA

51

# FIG. 35MM



M28 120 bp *FIG. 35NN* 

M 20:

XbaI SphI

CTATTGCACT GATAACGTGA AAACAAAGCA TTTGTTTCGT TCTAGAGCAT GCGTAGGAGA AAATAAATG AGATCTCGTA CGCATCCTCT TTTATTTTAC TTTATTTAC

Sapi

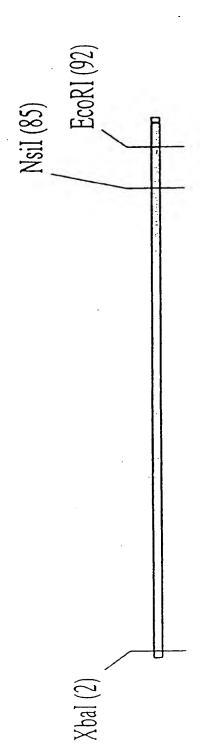
GGCACTCTTA CCGTTGCTCT TCACCCCTGT TACCAAAGCC GACTACAAAG CCGTGAGAAT GGCAACGAGA AGTGGGGACA ATGGTTTCGG CTGATGTTTC

51

MunI EcoRI

101 ATGAAGTGCA ATTGGAATTC TACTTCACGT TAACCTTAAG

# FIG. 3500



M21 96 bp *FIG. 35PP* 

M 21

XbaI

GAGGTGATTT TATGAAAAG AATATCGCAT TTCTTGC CTCCACTAAA ATACTTTTC TTATAGCGTA AAGAAGAACG TCTAGAGGTT AGATCTCCAA 1 1 1 1 1

NsiI

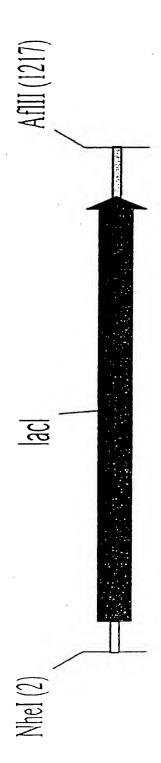
ECORI

GITITITICIA TIGCTACAAA TGCATACGCT GAATTC CAAAAAAGAT AACGATGTTT ACGTATGCGA CTTAAG

ATCTATGTTC TAGATACAAG

51

# FIG. 35QQ



M41 1221 bp *FIG.* 35RR

|   | • | • |
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|   |   |   |
| • | Σ |   |
| • | < | • |

NheI

| CAT GATAGCGCCC | GTA ACGTTATACG | TTC CCGCGTGGTG | AAAG TGGAAGCGGC | CAA CAACTGGCGG | TCT GGCCCTGCAC | SCCG ATCAACTGGG |
|----------------|----------------|----------------|-----------------|----------------|----------------|-----------------|
| GGTATGGCAT     | GAAACCAGTA     | AGACCGTTTC     | CGGGAAAAAG      | CGTGGCACAA     | CCTCCAGTCT     | TCTCGCGCCG      |
| CCATACCGTA     | CTTTGGTCAT     | TCTGGCAAAG     | GCCCTTTTTC      | GCACCGTGTT     | GGAGGTCAGA     |                 |
| AACCTTTCGC     | TGGTGAATGT     | GTCTCTTATC     | TGCGAAAACG      | TTCCTAACCG     | GGCGTTGCCA     | GGCGATTAAA      |
| TTGGAAAGCG     | ACCACTTACA     |                | ACGCTTTTGC      | AAGGATTGGC     | CCGCAACGGT     | CCGCTAATTT      |
| AATGGCGCAA     | CAATTCAGGG     | GTATGCCGGT     | GCCACGTTTC      | CTGAATTACA     | GTTGCTGATT     | AAATTGTCGC      |
| TTACCGCGTT     | GTTAAGTCCC     | CATACGGCCA     | CGGTGCAAAG      | GACTTAATGT     | CAACGACTAA     | TTTAACAGCG      |
| GCTAGCATCG     | GGAAGAGAGT     | ATGTCGCAGA     | AACCAGGCCA      | GATGGCGGAG     | GCAAACAGTC     | GCGCCGTCGC      |
| CGATCGTAGC     | CCTTCTCTCA     | TACAGCGTCT     | TTGGTCCGGT      | CTACCGCCTC     | CGTTTGTCAG     |                 |
|                | 51             | 101            | 151             | 201            | 251            | 301             |

## F/G, 35SS

| )                        | )<br>(<br>)<br>)<br>(<br>)<br>( |                          |                          |                          |     |
|--------------------------|---------------------------------|--------------------------|--------------------------|--------------------------|-----|
| TGCCATGTCC               | GCGACTGGAG<br>CGCTGACCTC        | GAACGGGAAG<br>CTTGCCCTTC | GCCGATAGCG<br>CGGCTATCGC | ATCAAATTCA<br>TAGTTTAAGT | 701 |
| CTCACTCGCA<br>GAGTGAGCGT | GCATAAATAT<br>CGTATTTATA        | TGGCTGGCTG<br>ACCGACCGAC | CGTCTGCGTC<br>GCAGACGCAG | TGTCTCGGCG               | 651 |
| CATTAAGTTC<br>GTAATTCAAG | TTAGCTGGCC<br>AATCGACCGG        | AATCGCGCTG<br>TTAGCGCGAC | GCCACCAGCA               | GTCGCATTGG<br>CAGCGTAACC | 601 |
| GGAGCATCTG<br>CCTCGTAGAC | GACTGGGCGT<br>CTGACCCGCA        | GACGGTACGC<br>CTGCCATGCG | CTCCCATGAG<br>GAGGGTACTC | GTATTATTT<br>CATAATAAAA  | 551 |
| CCCATCAACA<br>GGGTAGTTGT | TGACCAGACA<br>ACTGGTCTGT        | TTGATGTCTC<br>AACTACAGAG | GCGTTATTTC<br>CGCAATAAAG | TAATGTTCCG<br>ATTACAAGGC | 501 |
| CTGCCTGCAC               | GCTGTGGAAG<br>CGACACCTTC        | GGATGCTATT<br>CCTACGATAA | TGGATGACCA<br>ACCTACTGGT | AACTATCCGC<br>TTGATAGGCG | 451 |
| GCTGATTATT<br>CGACTAATAA | GTGTCAGTGG                      | CTCGCGCAAC<br>GAGCGCGTTG | GCACAATCTT<br>CGTGTTAGAA | AAGCGGCGGT<br>TTCGCCGCCA | 401 |
| GAAGCCTGTA<br>CTTCGGACAT | AAGCGGCGTC<br>TTCGCCGCAG        | TGGTAGAACG<br>ACCATCTTGC | GTCGTGTCGA               | TGCCAGCGTG<br>ACGGTCGCAC | 351 |

## FIG. 35TT

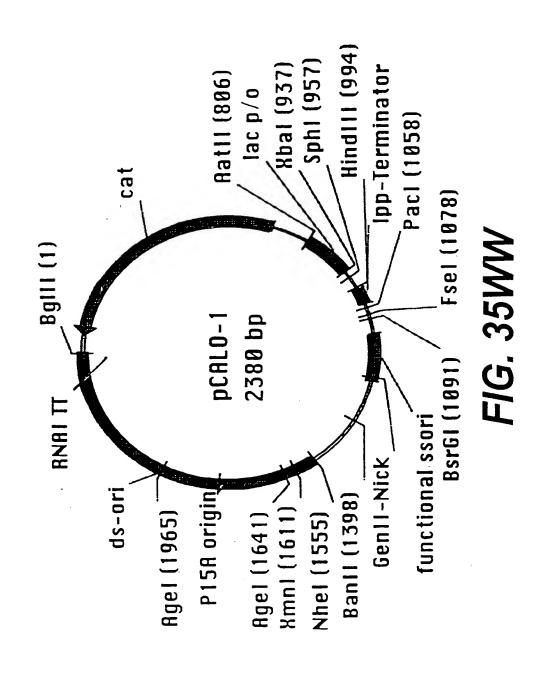
| 1   | 751  | GGTTTTCAAC<br>CCAAAAGTTG | AAACCATGCA<br>TTTGGTACGT | AATGCTGAAT<br>TTACGACTTA | GAGGGCATCG<br>CTCCCGTAGC | TTCCCACTGC<br>AAGGGTGACG |
|-----|------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| ω   | 301  | GATGCTGGTT<br>CTACGACCAA | GCCAACGATC<br>CGGTTGCTAG | AGATGGCGCT<br>TCTACCGCGA | GGGCGCAATG<br>CCCGCGTTAC | CGTGCCATTA<br>GCACGGTAAT |
| ω   | 851  | CCGAGTCCGG<br>GGCTCAGGCC | GCTGCGCGTT<br>CGACGCGCAA | GGTGCGGACA               | TCTCGGTAGT<br>AGAGCCATCA | GGGATACGAC<br>CCCTATGCTG |
| 01  | 901  | GATACCGAGG<br>CTATGGCTCC | ACAGCTCATG<br>TGTCGAGTAC | TTATATCCCG<br>AATATAGGGC | CCGCTGACCA               | CCATCAAACA<br>GGTAGTTTGT |
| 01  | 951  | GGATTTTCGC<br>CCTAAAAGCG | CTGCTGGGGC<br>GACGACCCCG | AAACCAGCGT<br>TTTGGTCGCA | GGACCGCTTG<br>CCTGGCGAAC | CTGCAACTCT<br>GACGTTGAGA |
| 7   | 001  | CTCAGGGCCA<br>GAGTCCCGGT | GGCGGTGAAG<br>CCGCCACTTC | GGCAATCAGC<br>CCGTTAGTCG | TGTTGCCCGT<br>ACAACGGGCA | CTCACTGGTG               |
| 1 ( | 1051 | AAAAGAAAAA<br>TTTTCTTTTT | CCACCCTGGC<br>GGTGGGACCG | TCCCAATACG<br>AGGGTTATGC | CAAACCGCCT<br>GTTTGGCGGA | CTCCCGCGC                |
| 7   | 101  | GTTGGCCGAT<br>CAACCGGCTA | TCACTGATGC<br>AGTGACTACG | AGCTGGCACG<br>TCGACCGTGC | ACAGGTTTCC<br>TGTCCAAAGG | CGACTGGAAA<br>GCTGACCTTT |

# FIG. 35UU

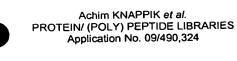
GCGGGCAGTG AGGCTACCCG ATAAAAGCGG CTTCCTGACA GGAGGCCGTT CGCCCGTCAC TCCGATGGGC TATTTTCGCC GAAGGACTGT CCTCCGGCAA 1151

Aflii

1201 TTGTTTTGCA GCCCACTTAA G AACAAAACGT CGGGTGAATT C FIG. 35VV







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|   |    |

| AAAAAATTA                                       | TTTTTTAAT                                       |
|-------------------------------------------------|-------------------------------------------------|
| PAGCAC CAGGCGTTTA AGGGCACCAA TAACTGCCTT AAAAAAA | GIG GICCGCAAAI ICCCGIGGIT AIIGACGGAA IITITITAAI |
| AGGCCACCAA                                      | TCCCGTGGTT                                      |
| CAGGCGTTTA                                      | GTG GTCCGCAAAT                                  |
| GATCTAGCAC                                      | CTAGATCGTG                                      |
| ⊣                                               |                                                 |

| TTAAGCATTC                                      | AATTCGTAAG                                      |
|-------------------------------------------------|-------------------------------------------------|
| CCC TGCCACTCAT CGCAGTACTG TTGTAATTCA TTAAGCATTC | GGG ACGGTGAGTA GCGTCATGAC AACATTAAGT AATTCGTAAG |
| CGCAGTACTG                                      | GCGTCATGAC                                      |
| TGCCACTCAT                                      | ACGGTGAGTA                                      |
| 2225222252                                      | 5555555555                                      |
| 51                                              |                                                 |

| CATG GAAGCCATCA CAAACGGCAT GATGAACCTG AATCGCCAGC | CTTCGGTAGT GTTTGCCGTA CTACTTGGAC TTAGCGGTCG |
|--------------------------------------------------|---------------------------------------------|
| GATGAACCTG                                       | CTACTTGGAC                                  |
| CAAACGGCAT                                       | GTTTGCCGTA                                  |
| GAAGCCATCA                                       | AC CTTCGGTAGT                               |
| TGCCGACATG                                       | ACGGCTGTAC                                  |
| 101                                              |                                             |

| AGCA CCTTGTCGCC TTGCGTATAA TATTTGCCCA TAGTGAAAAC | AACGGGT ATCACTTTTG                                |
|--------------------------------------------------|---------------------------------------------------|
| A CCTTGTCGCC TTGCGTATAA TATTTGCCCA TAGTG         | STCGT GGAACAGCGG AACGCATATT ATAAACGGGT ATCACTTTTG |
| TTGCGTATAA                                       | GCGG AACGCATATT ATAAAC                            |
| CCTTGTCGCC                                       | FICGT GGAACAGCGG                                  |
| GGCATCAGCA                                       | CCGTAGTCGT                                        |
| 151                                              |                                                   |

|--|

| CACCCA GGGATTGGCT GAGACGAAAA ACATATTCTC AATAAACCCT | TTATTGGGA                                        |
|----------------------------------------------------|--------------------------------------------------|
| ACATATTCTC                                         | reget cectaaces etergetiti tetataasas tratutessa |
| GAGACGAAAA                                         | CTCTGCTTTT                                       |
| GGGATTGGCT                                         | CCCTAACCGA                                       |
| AACTCACCCA                                         | TTGAGTGGGT                                       |
| 251                                                |                                                  |

| CTTGCGAATA               | GAACGCTTAT                                       |
|--------------------------|--------------------------------------------------|
| A CACGCCACAT CTTGCGAATA  | TITA ICCGGICCAA AAGIGGCAIT GIGCGGIGIA GAACGCITAI |
| STT TICACCGTAA C.        | AAGTGGCATT                                       |
| AT AGGCCAGGTT TTCACCGTAA | TCCGGTCCAA A                                     |
| TTAGGGAAAT               | AATCCCTTTA                                       |
| 301                      |                                                  |

## FIG. 35XX

| TC CAGAGCGATG            | NGG GTGAACACTA           | GA ACTCCGGGTG | GA TAAAACTTGT            | NTC CAGCTGAACG           | CT CAAAATGTTC            | CA GTGATTTTT<br>GT CACTAAAAAA | PAA CTCAAAAAAT<br>NTT GAGTTTTTTA |
|--------------------------|--------------------------|---------------|--------------------------|--------------------------|--------------------------|-------------------------------|----------------------------------|
| GTATTCACTC               | TGTAACAAGG               | GCCATACGGA    | AAAGGCCGGA               | CCGTAATATC               | TGAAATGCCT               | GGTATATCCA                    | ATCTCGATAA                       |
| CATAAGTGAG               | ACATTGTTCC               | CGGTATGCCT    | TTTCCGGCCT               | GGCATTATAG               | ACTTTACGGA               | CCATATAGGT                    | TAGAGCTATT                       |
| AATCGTCGTG<br>TTAGCAGCAC | TGGAAAACGG<br>ACCTTTTGCC | GTCTTTCATT    | GAATGTGAAT<br>CTTACACTTA | TTTAAAAAGG<br>AAATTTTTCC | AGCAACTGAC<br>TCGTTGACTG | TATCAACGGT                    | GCTCCTGAAA<br>CGAGGACTTT         |
| AACTGCCGGA               | AGTTTGCTCA               | CCAGCTCACC    | AGGCGGGCAA               | CTTTACGGTC               | AGGTACATTG               | CATTGGGATA                    | AGCTTCCTTA                       |
| TTGACGGCCT               | TCAAACGAGT               | GGTCGAGTGG    | TCCGCCCGTT               | GAAATGCCAG               | TCCATGTAAC               | GTAACCCTAT                    | TCGAAGGAAT                       |
| TATGTGTAGA               | AAAACGTTTC               | TCCCATATCA    | AGCATTCATC               | GCTTATTTTT               | GTCTGGTTAT               | TTTACGATGC                    | TCTCCATTTT                       |
| ATACACATCT               | TTTTGCAAAG               | AGGGTATAGT    | TCGTAAGTAG               | CGAATAAAAA               | CAGACCAATA               | AAATGCTACG                    | AGAGGTAAAA                       |
| 351                      | 401                      | 451           | 501                      | 551                      | 601                      | 651                           | 701                              |

# FIG. 35YY

| 751  | ACGCCCGGTA<br>TGCGGGCCAT | GTGATCTTAT<br>CACTAGAATA | TTCATTATGG<br>AAGTAATACC | TGAAAGTTGG<br>ACTTTCAACC | AACCTCACCC<br>TTGGAGTGGG |
|------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
|      | Aatii                    |                          |                          |                          |                          |
| 801  | GACGTCTAAT<br>CTGCAGATTA | GTGAGTTAGC<br>CACTCAATCG | TCACTCATTA<br>AGTGAGTAAT | GGCACCCCAG               | GCTTTACACT<br>CGAAATGTGA |
| 851  | TTATGCTTCC<br>AATACGAAGG | GGCTCGTATG<br>CCGAGCATAC | TTGTGTGGAA               | TTGTGAGCGG<br>AACACTCGCC | ATAACAATTT<br>TATTGTTAAA |
|      |                          |                          |                          | XbaI                     |                          |
| 901  | CACACAGGAA<br>GTGTGTCCTT | ACAGCTATGA<br>TGTCGATACT | CCATGATTAC<br>GGTACTAATG | GAATTTCTAG<br>CTTAAAGATC | ACCCCCCCCC               |
|      | Sphi                     |                          |                          |                          | HindIII                  |
| 951  | CGCATGCCAT<br>GCGTACGGTA | AACTTCGTAT<br>TTGAAGCATA | AATGTACGCT<br>TTACATGCGA | ATACGAAGTT<br>TATGCTTCAA | ATAAGCTTGA<br>TATTCGAACT |
| 1001 | CCTGTGAAGT<br>GGACACTTCA | GAAAAATGGC<br>CTTTTTACCG | GCAGATTGTG<br>CGTCTAACAC | CGACATTTTT<br>GCTGTAAAAA | TTTGTCTGCC<br>AAACAGACGG |

FIG. 35ZZ

# FIG. 35AAA

| AACTGCCCCT TICGGCGCT IGCACCGCTC AAGGAGCGGG CGCTAGGGCG CTGGCAAGTG TTCCTCGCCC GCGATCCCGC GACCGTTCAC ACCACCACAC CCGCCGCGCT TAATGCGCCG                                                            | GAGTGTATAC TGGCTTACTA TGTTGGCACT CTCACATATG ACCGAATGAT ACAACCGTGA                          | 0000<br>0000 | 1701 CTACGCTCGG TCGTTCGACT GCGGCGAGCG GAAATGGCTT ACGAACGGGG |      |                          |   | CGCCGCGCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG | CTGGCAAGTG GACCGTTCAC TAATGCGCGC ATTACGCGCCG ATTACGCACT ACAACCGTGA TTTCCGACGT CTTCCTCGCCT GAAGGAGCGA |                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------|-------------------------------------------------------------|------|--------------------------|---|----------------------------------------|------------------------------------------------------------------------------------------------------|--------------------------|
| Nhei  CGTGCTAGCG GAGTGTATAC TGGCTTACTA TGTTGGCACT  GCACGATCGC CTCACATATG ACCGAATGAT ACAACCGTGA  Xmni  TCAGTGAAGT GCTTCATGTG GCAGGAGAAA AAAGGCTGCA  AGTCACTTCA CGAAGTACAC CGTCCTCTT TTTCCGACGT | TCAGTGAAGT GCTTCATGTG GCAGGAGAAA AAAGGCTGCA<br>AGTCACTTCA CGAAGTACAC CGTCCTCTTT TTTCCGACGT |              |                                                             | 1651 | AGCAGAATAT<br>TCGTCTTATA | _ | ATATATTCCG<br>TATATAAGGC               | CTTCCTCGCT<br>GAAGGAGCGA                                                                             | CACTGACTCG<br>GTGACTGAGC |

| AA TGCTTGCCCC | SG GAAGTGAGAG<br>CC CTTCACTCTC | CT GACAAGCATC<br>GA CTGTTCGTAG | AC AGGACTATAA<br>TG TCCTGATATT | CT CTCCTGTTCC            | CG CGTTTGTCTC                              | SCT CCAAGCTGGA           | SCC TTATCCGGTA           |
|---------------|--------------------------------|--------------------------------|--------------------------------|--------------------------|--------------------------------------------|--------------------------|--------------------------|
| CTTTACCGAA    | ACTTAACAGG<br>TGAATTGTCC       | CCGCCCCCT                      | GAAACCCGAC<br>CTTTGGGCTG       | CTCCTGCGCT               | GTTATGGCCG                                 | GCAGTTCGCT<br>CGTCAAGCGA | CCGCTGCGCC               |
| CGCCGCTCGC    | CCAGGAAGAT<br>GGTCCTTCTA       | TCCATAGGCT<br>AGGTATCCGA       | CAGTGGTGGC<br>GTCACCACCG       | TGGCGGCTCC               | TCATTCCGCT                                 | TTCCGGGTAG<br>AAGGCCCATC | TTCAGTCCGA<br>AAGTCAGGCT |
| AGCAAGCTGA    | CTGGAAGATG<br>GACCTTCTAC       | AAGCCGTTTT<br>TTCGGCAAAA       | ACGCTCAAAT<br>TGCGAGTTTA       | CGTTTCCCCC               | Agel<br>~~~~~~<br>TTTACCGGTG<br>AAATGGCCAC | TGACACTCAG<br>ACTGTGAGTC | GAACCCCCCG               |
| GATGCGAGCC    | CGGAGATTTC<br>GCCTCTAAAG       | GGCCGCGGCA                     | ACGAAATCTG<br>TGCTTTAGAC       | AGATACCAGG<br>TCTATGGTCC | TGCCTTTCGG                                 | ATTCCACGCC<br>TAAGGTGCGG | CTGTATGCAC<br>GACATACGTG |
|               | 1751                           | 1801                           | 1851                           | 1901                     | 1951                                       | 2001                     | 2051                     |

FIG. 35CCC

|                              |                          | CATCTTATTA<br>GTAGAATAAT | TCAAGAAGAT<br>AGTTCTTCTA | CAAAACGATC<br>GTTTTGCTAG | 2351 |
|------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------|
|                              |                          | Bglii                    |                          |                          |      |
| r ACGCGCAGAC<br>A TGCGCGTCTG | GCAAGAGATT<br>CGTTCTCTAA | CGTTTTCAGA<br>GCAAAAGTCT | GCGGTTTTTT<br>CGCCAAAAAA | GCCCTGCAAG<br>CGGGACGTTC | 2301 |
| r acgaaaaacc<br>a tgctttttgg | CAGAGAACCT<br>GTCTCTTGGA | GTTGGTAGCT<br>CAACCATCGA | GGTTCAAAGA<br>CCAAGTTTCT | CAGTTACCTC               | 2251 |
| TCCTCCAAGC                   | GTGACTGCGC               | ACAAGTTTTA<br>TGTTCAAAAT | AACTGAAAGG<br>TTGACTTTCC | GTTAAGGCTA<br>CAATTCCGAT | 2201 |
| TCATGCGCCG                   | AGTCTTGAAG<br>TCAGAACTTC | TAGAGGAGTT<br>ATCTCCTCAA | GTAATTGATT<br>CATTAACTAA | GCAGCCACTG               | 2151 |
| CACACTGGCA                   | ATGCAAAAGC<br>TACGTTTTCG | CCGGAAAGAC<br>GGCCTTTCTG | TGAGTCCAAC<br>ACTCAGGTTG | ACTATCGTCT<br>TGATAGCAGA | 2101 |

FIG. 35DDD

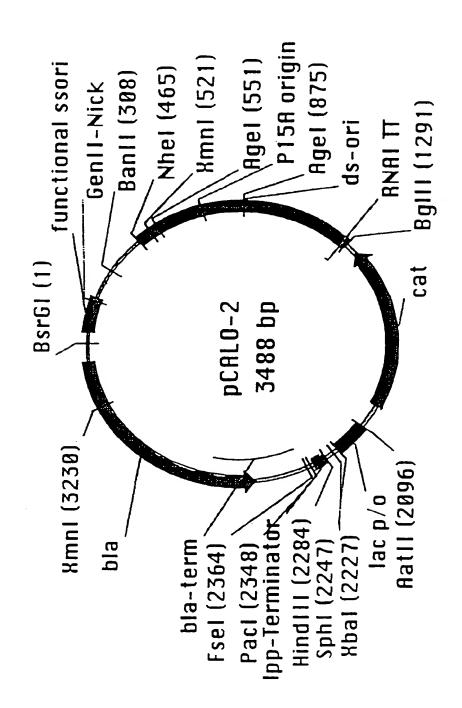


FIG. 35EEE

| . ← | GTACATGAAA                    | TTGTAAACGT | TAATATTTTG | TTAAAATTCG            | CGTTAAATTT |
|-----|-------------------------------|------------|------------|-----------------------|------------|
|     | CATGTACTTT                    | AACATTTGCA | ATTATAAAAC | AATTTTAAGC            | GCAATTTAAA |
| 51  | TTGTTAAATC                    | AGCTCATTTT | TTAACCAATA | GGCCGAAATC            | GGCAAAATCC |
|     | AACAATTTAG                    | TCGAGTAAAA | AATTGGTTAT | CCGGCTTTAG            | CCGTTTTAGG |
| 101 | CTTATAAATC                    | AAAAGAATAG | ACCGAGATAG | GGTTGAGTGT            | TGTTCCAGTT |
|     | GAATATTTAG                    | TTTTCTTATC | TGGCTCTATC | CCAACTCACA            | ACAAGGTCAA |
| 151 | TGGAACAAGA                    | GTCCACTATT | AAAGAACGTG | GACTCCAACG            | TCAAAGGGCG |
|     | ACCTTGTTCT                    | CAGGTGATAA | TTTCTTGCAC | CTGAGGTTGC            | AGTTTCCCGC |
| 201 | AAAAACCGTC                    | TATCAGGGCG | ATGGCCCACT | ACGAGAACCA            | TCACCCTAAT |
|     | TTTTTGGCAG                    | ATAGTCCCGC | TACCGGGTGA | TGCTCTTGGT            | AGTGGGATTA |
| 251 | CAAGTTTTTT                    | GGGGTCGAGG | TGCCGTAAAG | CACTAAATCG            | GAACCCTAAA |
|     | GTTCAAAAAA                    | CCCCAGCTCC | ACGGCATTTC | GTGATTTAGC            | CTTGGGATTT |
| 301 | Banii<br>~~~~~~<br>GGGAGCCCCC | GATTTAGAGC | TTGACGGGGA | TTGACGGGGA AAGCCGGCGA | ACGTGGCGAG |

FIG. 35FFF

| GAAATGGCTT               | GCGGCGAGCG               | TCGTTCGACT               | CTACGCTCGG                                | CACTGACTCG                                | 601 |
|--------------------------|--------------------------|--------------------------|-------------------------------------------|-------------------------------------------|-----|
| CTTCCTCGCT<br>GAAGGAGCGA | ATATATTCCG<br>TATATAAGGC | GTGATACAGG               | AGCAGAATAT<br>TCGTCTTATA                  | Agel<br>~~~~~<br>CCGGTGCGTC<br>GGCCACGCAG | 551 |
| AAAGGCTGCA<br>TTTCCGACGT | GCAGGAGAAA<br>CGTCCTCTTT | GCTTCATGTG               | TCAGTGAAGT<br>AGTCACTTCA                  | GATGAGGGTG                                | 501 |
| AgeI                     |                          | Ħ                        | Ym.                                       |                                           |     |
| TGTTGGCACT               | TGGCTTACTA               | GAGTGTATAC<br>CTCACATATG | Nhel<br>~~~~~<br>CGTGCTAGCG<br>GCACGATCGC | CTACAGGGCG                                | 451 |
| TAATGCGCCG<br>ATTACGCGGC | CCGCCGCGCT               | ACCACCACAC<br>TGGTGGTGTG | GCTGCGCGTA<br>CGACGCGCAT                  | TAGCGGTCAC                                | 401 |
| CTGGCAAGTG<br>GACCGTTCAC | CGCTAGGGCG<br>GCGATCCCGC | AAGGAGCGGG<br>TTCCTCGCCC | AAGAAAGCGA<br>TTCTTTCGCT                  | AAAGGAAGGG<br>TTTCCTTCCC                  | 351 |
| TGCACCGCTC               | Tregeceeer               | AACTGCCCCT               | CTAAATCTCG                                | CCCTCGGGGG                                |     |

FIG. 35GGG

| ATGCAAAAGC<br>TACGTTTTCG | AGTCTTGAAG<br>TCAGAACTTC | GTGACTGCGC               | CAGAGAACCT<br>GTCTCTTGGA | GCAAGAGATT<br>CGTTCTCTAA | Bglii<br>~~~~~~<br>GATCTAGCAC |                                                  |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-------------------------------|--------------------------------------------------|
| CCGGAAAGAC<br>GGCCTTTCTG | TAGAGGAGTT<br>ATCTCCTCAA | ACAAGTTTTA<br>TGTTCAAAAT | GTTĠGTAGCT<br>CAACCATCGA | CGTTTTCAGA<br>GCAAAAGTCT | ~<br>CATCTTATTA<br>GTAGAATAAT | AAAAAAATTA<br>TTTTTTAAT                          |
| TGAGTCCAAC<br>ACTCAGGTTG | GTAATTGATT<br>CATTAACTAA | AACTGAAAGG<br>TTGACTTTCC | GGTTCAAAGA<br>CCAAGTTTCT | GCGGTTTTTT<br>CGCCAAAAAA | TCAAGAAGAT<br>AGTTCTTCTA      | taactgcctt<br>attgacggaa<br><b>5111</b>          |
| ACTATCGTCT<br>TGATAGCAGA | GCAGCCACTG<br>CGTCGGTGAC | GTTAAGGCTA<br>CAATTCCGAT | CAGTTACCTC<br>GTCAATGGAG | GCCCTGCAAG<br>CGGGACGTTC | CAAAACGATC<br>GTTTTGCTAG      | AGGCCACCAA TAAC<br>TCCCGTGGTT ATTG<br>FIG. 35III |
| TTATCCGGTA<br>AATAGGCCAT | ACCACTGGCA<br>TGGTGACCGT | TCATGCGCCG               | TCCTCCAAGC<br>AGGAGGTTCG | ACGAAAAACC<br>TGCTTTTTGG | ACGCGCAGAC<br>TGCGCGTCTG      | CAGGCGTTTA                                       |
| 1001                     | 1051                     | 1101                     | 1151                     | 1201                     | 1251                          | 1301                                             |

| TTAAGCATTC TGCCGACATG        | AATCGCCAGC GGCATCAGCA | TAGTGAAAAC GGGGGGGGAAG       | AAACTGGTGA AACTCACCCA | AATAAACCCT TTAGGGAAAT | CTTGCGAATA TATGTGTAGA | CAGAGCGATG AAAACGTTTC        | GTGAACACTA TCCCATATCA        |
|------------------------------|-----------------------|------------------------------|-----------------------|-----------------------|-----------------------|------------------------------|------------------------------|
| AATTCGTAAG ACGGCTGTAC        | TTAGCGGTCG CCGTAGTCGT | ATCACTTTTG CCCCCGCTTC        | TTTGACCACT TTGAGTGGGT | TTATTTGGGA AATCCCTTTA | GAACGCTTAT ATACACATCT | GTCTCGCTAC TTTTGCAAAG        | CACTTGTGAT AGGGTATAGT        |
| TTGTAATTCA TTA               | GATGAACCTG AAT(       | TATTTGCCCA TAG               | GTTTAAATCA AAA(       | ACATATTCTC AAT.       | CACGCCACAT CTTO       | GTATTCACTC CAG               | TGTAACAAGG GTG               |
| AACATTAAGT AAT               | CTACTTGGAC TTA(       |                              | CAAATTTAGT TTT        | TGTATAAGAG TTA        | GTGCGGTGTA GAA        | CATAAGTGAG GTC               | ACATTGTTCC CAC               |
| CGCAGTACTG TTG               | AAACGGCAT             | TTGCGTATAA TAI               | TATTGGCTAC GTT        | GAGACGAAAA ACA        | TTCACCGTAA CAC        | AATCGTCGTG GTA               | TGGAAAACGG TG1               |
| GCGTCATGAC AAC               | TTTGCCGTA             | AACGCATATT ATA               | ATAACCGATG CAA        | CTCTGCTTTT TG1        | AAGTGGCATT GTC        | TTAGCAGCAC CAI               | ACCTTTTGCC AC2               |
| TGCCACTCAT C<br>ACGGTGAGTA G | GAAGCCATCA CL         | CCTTGTCGCC T<br>GGAACAGCGG A | AAGTTGTCCA T          | GGGATTGGCT G          | AGGCCAGGTT I          | AACTGCCGGA A<br>TTGACGGCCT I | AGTTTGCTCA T<br>TCAAACGAGT A |
| 1,351                        | 1401                  | 1451                         | 1501                  | 1551                  | 1601                  | 1651                         | 1701                         |

FIG. 35JJJ

|                                             |                          | FIG. 35KKK               | FIG.       |            |      |
|---------------------------------------------|--------------------------|--------------------------|------------|------------|------|
| TTATGCTTCC                                  | GCTTTACACT               | GGCACCCCAG               | TCACTCATTA | GTGAGTTAGC | 2101 |
| Aatii<br>~~~~~~<br>GACGTCTAAT<br>CTGCAGATTA | AACCTCACCC<br>TTGGAGTGGG | TGAAAGTTGG<br>ACTTTCAACC | TTCATTATGG | GTGATCTTAT | 2051 |
| ACGCCCGGTA                                  | CTCAAAAAAT               | ATCTCGATAA               | GCTCCTGAAA | AGCTTCCTTA | 2001 |
| TGCGGGCCAT                                  | GAGTTTTTTA               | TAGAGCTATT               | CGAGGACTTT | TCGAAGGAAT |      |
| TCTCCATTTT                                  | GTGATTTTTT               | GGTATATCCA               | TATCAACGGT | CATTGGGATA | 1951 |
| AGAGGTAAAA                                  | CACTAAAAAA               | CCATATAGGT               | ATAGTTGCCA | GTAACCCTAT |      |
| TTTACGATGC                                  | CAAAATGTTC               | TGAAATGCCT               | AGCAACTGAC | AGGTACATTG | 1901 |
| AAATGCTACG                                  | GTTTTACAAG               | ACTTTACGGA               | TCGTTGACTG | TCCATGTAAC |      |
| GTCTGGTTAT                                  | CAGCTGAACG               | CCGTAATATC               | TTTAAAAAGG | CTTTACGGTC | 1851 |
| CAGACCAATA                                  | GTCGACTTGC               | GGCATTATAG               | AAATTTTTCC | GAAATGCCAG |      |
| GCTTATTTT                                   | TAAAACTTGT               | AAAGGCCGGA               | GAATGTGAAT | AGGCGGGCAA | 1801 |
| CGAATAAAAA                                  | ATTTTGAACA               | TTTCCGGCCT               | CTTACACTTA | TCCGCCCGTT |      |
| AGCATTCATC                                  | ACTCCGGGTG               | GCCATACGGA               | GTCTTTCATT | CCAGCTCACC | 1751 |
| TCGTAAGTAG                                  | TGAGGCCCCAC              | CGGTATGCCT               | CAGAAAGTAA | GGTCGAGTGG |      |

|      | CACTCAATCG               | AGTGAGTAAT               | CCGTGGGGTC                                 | CGAAATGTGA                                    | AATACGAAGG                                  |
|------|--------------------------|--------------------------|--------------------------------------------|-----------------------------------------------|---------------------------------------------|
| 2151 | GGCTCGTATG<br>CCGAGCATAC | TTGTGTGGAA<br>AACACACCTT | TTGTGAGCGG<br>AACACTCGCC                   | ATAACAATTT<br>TATTGTTAAA                      | CACACAGGAA<br>GTGTGTCCTT                    |
| 2201 | ACAGCTATGA<br>TGTCGATACT | CCATGATTAC<br>GGTACTAATG | Xbal<br>ZZZZZZ<br>GAATTTCTAG<br>CTTAAAGATC | .~<br>Acccccccc<br>TGGGGGGGG                  | Sphi<br>cccarccar<br>cccarccar              |
| 2251 | AACTTCGTAT<br>TTGAAGCATA | AATGTACGCT<br>TTACATGCGA | ATACGAAGTT<br>TATGCTTCAA                   | HindIII<br>~~~~~~<br>ATAAGCTTGA<br>TATTCGAACT | CCTGTGAAGT<br>GGACACTTCA                    |
| 2301 | GAAAAATGGC<br>CTTTTTACCG | GCAGATTGTG<br>CGTCTAACAC | CGACATTTTT<br>GCTGTAAAAA                   | TTTGTCTGCC                                    | PacI<br>~~~~~~~<br>GTTTAATTAA<br>CAAATTAATT |
| 2351 | Fs                       | FseI                     | CAAAAAGGAT<br>GTTTTTCCTA                   | CTCAAGAAGA                                    | TCCTTTGATC                                  |

FIG. 35LLL

| CATCCAGTCT<br>GTAGGTCAGA | TATCCGCCTC<br>ATAGGCGGAG | CCTGCAACTT<br>GGACGTTGAA | CAGAAGTGGT  | GGGCCGAGCG<br>CCCGGCTCGC | 2751 |
|--------------------------|--------------------------|--------------------------|-------------|--------------------------|------|
| CCAGCCGGAA               | AATAAACCAG               | ATTTATCAGC               | CCGCCTCCAG  | CCCACGCTCA               | 2701 |
| GGTCGGCCTT               | TTATTTGGTC               | TAAATAGTCG               | GGCCGAGGTC  | GGGTGCGAGT               |      |
| TACCGCGAGA               | GCTGCAATGA               | TGGCCCCAGT               | GCTTACCATC  | ATACGGGAGG               | 2651 |
| ATGGCGCTCT               | CGACGTTACT               | ACCGGGGTCA               | CGAATGGTAG  | TATGCCCTCC               |      |
| GATAACTACG               | CCGTCGTGTA               | GCCTGACTCC               | ATCCATAGTT  | TATTTCGTTC               | 2601 |
| CTATTGATGC               | GGCAGCACAT               | CGGACTGAGG               | TAGGTATCAA  | ATAAAGCAAG               |      |
| GCGATCTGTC               | ACCTATCTCA               | TCAGTGAGGC               | CAATGCT'TAA | GACAGTTACC               | 2551 |
| CGCTAGACAG               | TGGATAGAGT               | AGTCACTCCG               | GTTACGAATT  | CTGTCAATGG               |      |
| AACTTGGTCT               | TATATGAGTA               | ATCTAAAGTA               | TTTTAAATCA  | AAAAATGAAG               | 2501 |
| TTGAACCAGA               | ATATACTCAT               | TAGATTTCAT               | AAAATTTAGT  | TTTTTACTTC               |      |
| CTTTTAAATT               | CACCTAGATC               | AAAGGATCTT               | AGATTATCAA  | TTTGGTCATG               | 2451 |
| GAAAATTTAA               | GTGGATCTAG               | TTTCCTAGAA               | TCTAATAGTT  | AAACCAGTAC               |      |
| GTTAAGGGAT               | GAAAACTCAC               | TCAGTGGAAC               | GGTCTGACGC  | TTTTCTACGG               | 2401 |
| CAATTCCCTA               | CTTTTGAGTG               | AGTCACCTTG               | CCAGACTGCG  | AAAAGATGCC               |      |

# FIG. 35MMM

| TTAATAGTTT               | CGCTCGTCGT               | GCGAGTTACA               | GTCCTCCGAT               | GTTATGGCAG               | CTTTTCTGTG               | TGCGGCGACC               | CCACATAGCA               |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| AATTATCAAA               | GCGAGCAGCA               | CGCTCAATGT               |                          | CAATACCGTC               | GAAAAGACAC               | ACGCCGCTGG               | GGTGTATCGT               |
| AGTTCGCCAG               | CGTGGTGTCA               | AACGATCAAG<br>TTGCTAGTTC | AGCTCCTTCG<br>TCGAGGAAGC | ATCACTCATG               | CCGTAAGATG               | GAATAGTGTA<br>CTTATCACAT | TAATACCGCG<br>ATTATGGCGC |
| TAGAGTAAGT               | CTACAGGCAT               | TCCGGTTCCC               | AAAAGCGGTT               | CCGCAGTGTT               | GTCATGCCAT               | GTCATTCTGA               | CAATACGGGA               |
| ATCTCATTCA               | GATGTCCGTA               | AGGCCAAGGG               | TTTTCGCCAA               | GGCGTCACAA               |                          | CAGTAAGACT               | GTTATGCCCT               |
| GCCGGGAAGC               | GTTGCCATTG               | TTCATTCAGC               | TGTTGTGCAA               | AGTAAGTTGG               | TTCTCTTACT               | ACTCAACCAA               | TGCCCGGCGT               |
| CGGCCCTTCG               | CAACGGTAAC               | AAGTAAGTCG               | ACAACACGTT               | TCATTCAACC               | AAGAGAATGA               | TGAGTTGGTT               | ACGGGCCGCA               |
| ATTAACTGTT<br>TAATTGACAA | GCGCAACGTT<br>CGCGTTGCAA | TTGGTATGGC               | TGATCCCCCA               | CGTTGTCAGA<br>GCAACAGTCT | CACTGCATAA<br>GTGACGTATT | ACTGGTGAGT<br>TGACCACTCA | GAGTTGCTCT<br>CTCAACGAGA |
| 2801                     | 2851                     | 2901                     | 2951                     | 3001                     | 3051                     | 3101                     | 3151                     |

1

FIG. 35NNN

## XmnI

| GAAGCATTTA | CAATATTATT | CTTCCTTTTT | TACTCATACT | AAATGTTGAA | 3401 |
|------------|------------|------------|------------|------------|------|
| CTTCGTAAAT | GTTATAATAA | GAAGGAAAAA | ATGAGTATGA | TTTACAACTT |      |
| GGCGACACGG | AGGGAATAAG | GCCGCAAAAA | AAGGCAAAAT | CAAAAACAGG | 3351 |
| CCGCTGTGCC | TCCCTTATTC | CGGCGTTTTT | TTCCGTTTTA | GTTTTTGTCC |      |
| TCTGGGTGAG | CACCAGCGTT | CTTTTACTTT | TCCTCAGCAT | ACCCAACTGA | 3301 |
| AGACCCACTC | GTGGTCGCAA | GAAAATGAAA | AGGAGTCGTA | TGGGTTGACT |      |
| CCACTCGCGC | TCGATGTAAC | GAGATCCAGT | TACCGCTGTT | TCAAGGATCT | 3251 |
| GGTGAGCGCG | AGCTACATTG | CTCTAGGTCA | ATGGCGACAA | AGTTCCTAGA |      |
| GCGAAAACTC | GTTCTTCGGG | ATTGGAAAAC | AGTGCTCATC | GAACTTTAAA | 3201 |
| CGCTTTTGAG | CAAGAAGCCC | TAACCTTTTG | TCACGAGTAG | CTTGAAATTT |      |

## BsrGI

TCAGGGTTAT TGTCTCATGA GCGGATACAT ATTTGAAT AGTCCCAATA ACAGAGTACT CGCCTATGTA TAAACTTA 3451

# FIG. 35000

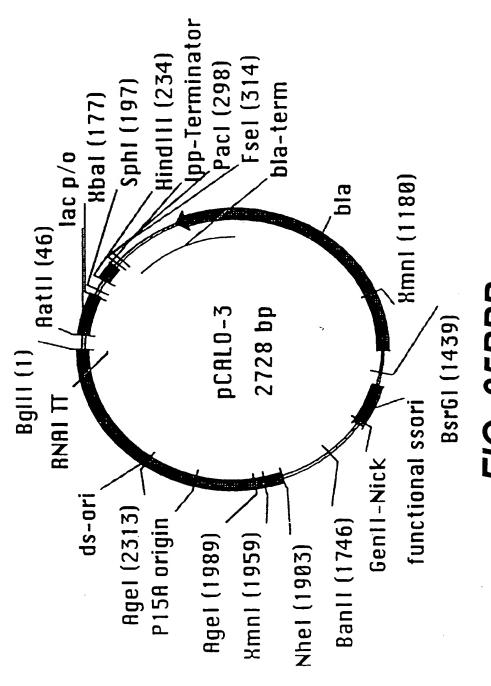


FIG. 35PPP

| Aatii           | GACGTCTAAT<br>CTGCAGATTA | TTATGCTTCC<br>AATACGAAGG  | CACACAGGAA<br>GTGTGTCCTT | Sphi<br>~~~~~~<br>CGCATGCCAT<br>GCGTACGGTA | CCTGTGAAGT<br>GGACACTTCA                      |
|-----------------|--------------------------|---------------------------|--------------------------|--------------------------------------------|-----------------------------------------------|
|                 | ACGAAGTTAT<br>TGCTTCAATA | GCTTTACACT<br>CGAAATGTGA  | ATAACAATTT<br>TATTGTTAAA | ACCCCCCCC<br>TGGGGGGGG                     | HindIII<br>~~~~~~<br>ATAAGCTTGA<br>TATTCGAACT |
|                 | TGTATGCTAT<br>ACATACGATA | GGCACCCCAG<br>CCGTGGGGGTC | TTGTGAGCGG               | XbaI<br>~~~~~<br>GAATTTCTAG<br>CTTAAAGATC  | ATACGAAGTT<br>TATGCTTCAA                      |
|                 | CTTCGTATAA<br>GAAGCATATT | TCACTCATTA<br>AGTGAGTAAT  | TTGTGTGGAA<br>AACACACCTT | CCATGATTAC<br>GGTACTAATG                   | AATGTACGCT<br>TTACATGCGA                      |
| O-3:<br>BglII   | GATCTCATAA<br>CTAGAGTATT | GTGAGTTAGC<br>CACTCAATCG  | GGCTCGTATG<br>CCGAGCATAC | ACAGCTATGA<br>TGTCGATACT                   | AACTTCGTAT<br>TTGAAGCATA                      |
| pCALO-3:<br>Bgl | <del>, - 1</del>         | 51                        | 101                      | 151                                        | 201                                           |

PacI

| . 251 | GAAAAATGGC (             | GCAGATTGTG<br>CGTCTAACAC | CGACATTTTT<br>GCTGTAAAAA | TTTGTCTGCC<br>AAACAGACGG | GTTTAATTAA<br>CAAATTAATT         |
|-------|--------------------------|--------------------------|--------------------------|--------------------------|----------------------------------|
|       | H<br>B<br>B<br>B         | S I                      |                          |                          |                                  |
| 301   | 90<br>00                 | $\mathcal{O}$            | CAAAAAGGAT<br>GTTTTTCCTA | CTCAAGAAGA<br>GAGTTCTTCT | TCCTTTGATC<br>AGGAAACTAG         |
| 351   | TTTTCTACGG AAAAGATGCC    | GGTCTGACGC<br>CCAGACTGCG | TCAGTGGAAC               | GAAAACTCAC<br>CTTTTGAGTG | <b>GTTAAG</b> GGAT<br>CAATTCCCTA |
| 401   | TTTGGTCATG               | AGATTATCAA<br>TCTAATAGTT | AAAGGATCTT<br>TTTCCTAGAA | CACCTAGATC<br>GTGGATCTAG | CTTTTAAATT<br>GAAAATTTAA         |
| 451   | AAAAATGAAG<br>TTTTTACTTC | TTTTAAATCA<br>AAAATTTAGT | ATCTAAAGTA<br>TAGATTTCAT | TATATGAGTA<br>ATATACTCAT | AACTTGGTCT<br>TTGAACCAGA         |
| 501   | GACAGTTACC               | CAATGCTTAA<br>GTTACGAATT | TCAGTGAGGC<br>AGTCACTCCG | ACCTATCTCA<br>TGGATAGAGT | GCGATCTGTC<br>CGCTAGACAG         |
| 551   | TATTTCGTTC               | ATCCATAGTT<br>TAGGTATCAA | GCCTGACTCC<br>CGGACTGAGG | CCGTCGTGTA<br>GGCAGCACAT | GATAACTACG<br>CTATTGATGC         |
|       |                          | FIG. 35RRR               | <b>5RRR</b>              |                          |                                  |

| 601 | ATACGGGAGG<br>TATGCCCTCC | GCTTACCATC<br>CGAATGGTAG | TGGCCCCAGT               | GCTGCAATGA<br>CGACGTTACT | TACCGCGAGA<br>ATGGCGCTCT |
|-----|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 651 | CCCACGCTCA               | CCGGCTCCAG<br>GGCCGAGGTC | ATTTATCAGC<br>TAAATAGTCG | AATAAACCAG<br>TTATTTGGTC | CCAGCCGGAA<br>GGTCGGCCTT |
| 701 | GGGCCGAGCG               | CAGAAGTGGT<br>GTCTTCACCA | CCTGCAACTT<br>GGACGTTGAA | TATCCGCCTC<br>ATAGGCGGAG | CATCCAGTCT<br>GTAGGTCAGA |
| 751 | ATTAACTGTT               | GCCGGGAAGC               | TAGAGTAAGT               | AGTTCGCCAG               | TTAATAGTTT               |
|     | TAATTGACAA               | CGGCCCTTCG               | ATCTCATTCA               | TCAAGCGGTC               | AATTATCAAA               |
| 801 | GCGCAACGTT               | GTTGCCATTG               | CTACAGGCAT               | CGTGGTGTCA               | CGCTCGTCGT               |
|     | CGCGTTGCAA               | CAACGGTAAC               | GATGTCCGTA               | GCACCACAGT               | GCGAGCAGCA               |
| 851 | TTGGTATGGC               | TTCATTCAGC               | TCCGGTTCCC               | AACGATCAAG               | GCGAGTTACA               |
|     | AACCATACCG               | AAGTAAGTCG               | AGGCCAAGGG               | TTGCTAGTTC               | CGCTCAATGT               |
| 901 | TGATCCCCCA               | TGTTGTGCAA               | AAAAGCGGTT               | AGCTCCTTCG               | GTCCTCCGAT               |
|     | ACTAGGGGGT               | ACAACACGTT               | TTTTCGCCAA               | TCGAGGAAGC               | CAGGAGGCTA               |
| 951 | CGTTGTCAGA               | AGTAAGTTGG               | CCGCAGTGTT               | ATCACTCATG               | GTTATGGCAG               |
|     | GCAACAGTCT               | TCATTCAACC               | GGCGTCACAA               | TAGTGAGTAC               | CAATACCGTC               |

## FIG. 35SSS

| 1001 | CACTGCATAA               | TTCTCTTACT                            | GTCATGCCAT               | CCGTAAGATG               | CTTTTCTGTG               |
|------|--------------------------|---------------------------------------|--------------------------|--------------------------|--------------------------|
| 1201 |                          | A A A A A A A A A A A A A A A A A A A | ないというようない                | GAPTAGTA                 |                          |
|      | TGACCACTCA               | TGAGTTGGTT                            | CAGTAAGACT               | CTTATCACAT               | ACGCCGCTGG               |
| 1101 | GAGTTGCTCT<br>CTCAACGAGA | TGCCCGGCGT                            | CAATACGGGA<br>GTTATGCCCT | TAATACCGCG<br>ATTATGGCGC | CCACATAGCA<br>GGTGTATCGT |
|      |                          |                                       | Xmn I                    |                          |                          |
| 1151 | GAACTTTAAA               | AGTGCTCATC<br>TCACGAGTAG              | ATTGGAAAAC<br>TAACCTTTTG | GTTCTTCGGG<br>CAAGAAGCCC | GCGAAAACTC<br>CGCTTTTGAG |
| 1201 | TCAAGGATCT<br>AGTTCCTAGA | TACCGCTGTT<br>ATGGCGACAA              | GAGATCCAGT<br>CTCTAGGTCA | TCGATGTAAC<br>AGCTACATTG | CCACTCGCGC<br>GGTGAGCGCG |
| 1251 | ACCCAACTGA<br>TGGGTTGACT | TCCTCAGCAT<br>AGGAGTCGTA              | CTTTTACTTT<br>GAAAATGAAA | CACCAGCGTT<br>GTGGTCGCAA | TCTGGGTGAG<br>AGACCCACTC |
| 1301 | CAAAAACAGG<br>GTTTTTGTCC | AAGGCAAAAT<br>TTCCGTTTTA              | GCCGCAAAAA<br>CGGCGTTTTT | AGGGAATAAG<br>TCCCTTATTC | GGCGACACGG<br>CCGCTGTGCC |
| 1351 | AAATGTTGAA               | TACTCATACT                            | CTTCCTTTT                | CAATATTATT               | GAAGCATTTA               |

FIG. 35TTT

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| T ATG         |
| T ATG         |

## BsrGI

| 1401 | TCAGGGTTAT | TGTCTCATGA<br>ACAGAGTACT | GCGGATACAT<br>CGCCTATGTA | ATTTGAATGT<br>TAAACTTACA | ACATGAAATT<br>TGTACTTTAA |
|------|------------|--------------------------|--------------------------|--------------------------|--------------------------|
| 1451 | GTAAACGTTA | ATATTTTGTT               | AAAATTCGCG               | TTAAATTTTT               | GTTAAATCAG               |
|      | CATTTGCAAT | TATAAAACAA               | TTTTAAGCGC               | AATTTAAAAA               | CAATTTAGTC               |
| 1501 | CTCATTTTTT | AACCAATAGG               | CCGAAATCGG               | CAAAATCCCT               | TATAAATCAA               |
|      | GAGTAAAAAA | TTGGTTATCC               | GGCTTTAGCC               | GTTTTAGGGA               | ATATTTAGTT               |
| 1551 | AAGAATAGAC | CGAGATAGGG               | TTGAGTGTTG               | TTCCAGTTTG               | GAACAAGAGT               |
|      | TTCTTATCTG | GCTCTATCCC               | AACTCACAAC               | AAGGTCAAAC               | CTTGTTCTCA               |
| 1601 | CCACTATTAA | AGAACGTGGA               | CTCCAACGTC               | AAAGGGCGAA               | AAACCGTCTA               |
|      | GGTGATAATT | TCTTGCACCT               | GAGGTTGCAG               | TTTCCCGCTT               | TTTGGCAGAT               |
| 1651 | TCAGGGCGAT | GGCCCACTAC               | GAGAACCATC               | ACCCTAATCA               | AGTTTTTGG                |
|      | AGTCCCGCTA | CCGGGTGATG               | CTCTTGGTAG               | TGGGATTAGT               | TCAAAAAACC               |

BanlI

| 1701 | GGTCGAGGTG<br>CCAGCTCCAC                   | CCGTAAAGCA<br>GGCATTTCGT | CTAAATCGGA<br>GATTTAGCCT | ACCCTAAAGG<br>TGGGATTTCC | GAGCCCCCGA<br>CTCGGGGGCT       |
|------|--------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------------|
| 1751 | TTTAGAGCTT<br>AAATCTCGAA                   | GACGGGGAAA<br>CTGCCCCTTT | GCCGGCGAAC<br>CGGCCGCTTG | GTGGCGAGAA<br>CACCGCTCTT | AGGAAGGGAA<br>TCCTTCCCTT       |
| 1801 | GAAAGCGAAA<br>CTTTCGCTTT                   | GGAGCGGGCG<br>CCTCGCCCGC | CTAGGGCGCT<br>GATCCCGCGA | GGCAAGTGTA<br>CCGTTCACAT | GCGGTCACGC<br>CGCCAGTGCG       |
| 1851 | TGCGCGTAAC<br>ACGCGCATTG                   | CACCACACCC<br>GTGGTGTGGG | GCCGCGCTTA<br>CGGCGCGAAT | ATGCGCCGCT               | ACAGGGCGCG<br>TGTCCCGCGC       |
| 1901 | NheI<br>~~~~~~<br>TGCTAGCGGA<br>ACGATCGCCT | GTGTATACTG               | GCTTACTATG<br>CGAATGATAC | TTGGCACTGA               | TGAGGGTGTC<br>ACTCCCACAG       |
|      |                                            |                          |                          | Age                      | I                              |
| 1951 | AGTGAAGTGC<br>TCACTTCACG                   | TTCATGTGGC               | AGGAGAAAAA<br>TCCTCTTTTT | AGGCTGCACC<br>TCCGACGTGG | cc ggrgcgrcag<br>gg ccacgcagrc |
| 2001 | CAGAATATGT<br>GTCTTATACA                   | GATACAGGAT<br>CTATGTCCTA | ATATTCCGCT               | TCCTCGCTCA<br>AGGAGCGAGT | CTGACTCGCT<br>GACTGAGCGA       |
|      |                                            | FIG. 35VVV               | 5WV                      |                          |                                |

# FIG. 35WWW

| 2401 | GTATGCACGA | ACCCCCCGTT | CAGTCCGACC | GCTGCGCCTT | ATCCGGTAAC |
|------|------------|------------|------------|------------|------------|
|      | CATACGTGCT | TGGGGGGCAA | GTCAGGCTGG | CGACGCGGAA | TAGGCCATTG |
| 2451 | TATCGTCTTG | AGTCCAACCC | GGAAAGACAT | GCAAAAGCAC | CACTGGCAGC |
|      | ATAGCAGAAC | TCAGGTTGGG | CCTTTCTGTA | CGTTTTCGTG | GTGACCGTCG |
| 2501 | AGCCACTGGT | AATTGATTTA | GAGGAGTTAG | TCTTGAAGTC | ATGCGCCGGT |
|      | TCGGTGACCA | TTAACTAAAT | CTCCTCAATC | AGAACTTCAG | TACGCGGCCA |
| 2551 | TAAGGCTAAA | CTGAAAGGAC | AAGTTTTAGT | GACTGCGCTC | CTCCAAGCCA |
|      | ATTCCGATTT | GACTTTCCTG | TTCAAAATCA | CTGACGCGAG | GAGGTTCGGT |
| 2601 | GTTACCTCGG | TTCAAAGAGT | TGGTAGCTCA | GAGAACCTAC | GAAAAACCGC |
|      | CAATGGAGCC | AAGTTTCTCA | ACCATCGAGT | CTCTTGGATG | CTTTTTGGCG |
| 2651 | CCTGCAAGGC | GGTTTTTTCG | TTTCAGAGC  | AAGAGATTAC | GCGCAGACCA |
|      | GGACGTTCCG | CCAAAAAAGC | AAAAGTCTCG | TTCTCTAATG | CGCGTCTGGT |

AAACGATCTC AAGAAGATCA TCTTATTA TTTGCTAGAG TTCTTCTAGT AGAATAAT

2701

Bglii

## FIG. 35XXX

M1: PCR using template

NoVspAatII: TAGACGTC

M2: synthesis

BloxA-A: TATGAGATCTCATAACTTCGTATAATGTACGCTATACG-

**AAGTTAT** 

BloxA-B: TAATAACTTCGTATAGCATACATTATACGAAGTTATG-

**AGATCTCA** 

M3: PCR, NoVspAatII as second oligo

XloxS-muta: CATTTTTGCCCTCGTTATCTACGCATGCGATAACTTCGTA-TAGCGTACATTATACGAAGTTATTCTAGACATGGTCATAGCTGTTTCCTG

M7-1: PCR

gIIINEW-fow: GGGGGGAATTCGGTGGTGGTGGATCTGCGTGCGCTG-

AAACGGTTGAAAGTTG

gIIINEW-rev: CCCCCCAAGCTTATCAAGACTCCTTATTACG

M7-II: PCR

glllss-fow: GGGGGGGAATTCGGAGGCGGTTCCGGTGGTGGC

M7-III: PCR

glllsupernew-fow: GGGGGGGGAATTCGAGCAGAAGCTGATCTCT-GAGGAGGATCTGTAGGGTGGTGGCTCTGGTTCCGGTGATTTTG

FIG. 35YYY

M8: synthesis

Iox514-A: CCATAACTTCGTATAATGTACGCTATACGAAGTTATA

IOX514-B: AGCITATAACTTCGTATAGCGTACATTATACGAAGT-

**TATGGCATG** 

M9II: synthesis

M9II-fow: AGCTTGACCTGTGAAGTGAAAAATGGCGCAGATT-

M9II-rev: GTACACCCCCCCCAGGCCGGCCCCCCCCCTTTAA-

TTAAACGGCAGACAAAAAAAAATGTCGCACAATCTGCG

M10II: assembly PCR with template

bla-fow: GGGGGGGTGTACATTCAAATATGTATCCGCTCATG

bla-seq4: GGGTTACATCGAACTGGATCTC

bla1-muta: CCAGTTCGATGTAACCCACTCGCGCACCCAACTGATC-

CTCAGCATCTTTTACTTTCACC

blall-muta: ACTCTAGCTTCCCGGCAACAGTTAATAGACTGGATG-

**GAGGCGG** 

bla-NEW: CTGTTGCCGGGAAGCTAGAGTAAG

bla-rev: CCCCCCTTAATTAAGGGGGGGGGCCGGCCATTATCAAA-

AAGGATCTCAAGAAGATCC

M11II/III: PCR, site-directed mutagenesis

FIG. 35ZZZ

f1-fow: GGGGGGGCTAGCACGCCCCTGTAGCGGCGCATTAA

f1-rev: CCCCCCTGTACATGAAATTGTAAACGTTAATATTTTG

f1-t133.muta: GGGCGATGGCCCACTACGAGAACCATCACCCTAATC

M12: assembly PCR using template

p15-fow: GGGGGGAGATCTAATAAGATGATCTTCTTGAG

p15-NEWI: GAGTTGGTAGCTCAGAGAACCTACGAAAAACCGCCCTG-

**CAAGGCG** 

p15-NEWII: GTAGGTTCTCTGAGCTACCAACTC

p15-NEWIII: GTTTCCCCCTGGCGGCTCCCTCCTGCGCTCTCCTGTTCCT-

GCC

p15-NEWIV: AGGAGGGAGCCGCCAGGGGAAAC

p15-rev: GACATCAGCGCTAGCGGAGTGTATAC

M13: synthesis

BloxXB-A: GATCTCATAACTTCGTATAATGTATGCTATACGAAGTTA-

TTCA

BloxXB-B: GATCTGAATAACTTCGTATAGCATACATTATACGAAGTTA-

**TGAGA** 

M14-Ext2: PCR, site-directed mutagenesis

ColEXT2-fow: GGGGGGGAGATCTGACCAAAATCCCTTAACGTGAG

Col-mutal: GGTATCTGCGCTCTGCTGTAGCCAGTTACCTTCGG

FIG. 35AAAA

Col-rev: CCCCCCGCTAGCCATGTGAGCAAAAGGCCAGCAA

M17: assembly PCR using template

CAT-1: GGGACGTCGGGTGAGGTTCCAAC

CAT-2: CCATACGGAACTCCGGGTGAGCATTCATC

CAT-3: CCGGAGTTCCGTATGG

CAT-4: ACGTTTAAATCAAAACTGG

CAT-5: CCAGTTTTGATTTAAACGTAGCCAATATGGACAACTTCTTC-

GCCCCGTTTTCACTATGGGCAAATATT

CAT-6: GGAAGATCTAGCACCAGGCGTTTAAG

M41: assembly PCR using template

LAC1: GAGGCCGGCCATCGAATGGCGCAAAAC

LAC2: CGCGTACCGTCCTCATGGGAGAAAATAATAC

LAC3: CCATGAGGACGGTACGCGACTGGGCGTGGAGCATCTGGTCGCA-

TTGGGTCACCAGCAAATCCGCTGTTAGCTGGCCCATTAAG

LAC4: GTCAGCGGCGGGATATAACATGAGCTGTCCTCGGTATCGTCG

LAC5: GTTATATCCCGCCGCTGACCACCATCAAAC

LAC6: CATCAGTGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGT4TTG-

**GGAGCCAGGGTGGTTTTTC** 

LAC7: GGTTAATTAACCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCC-

AGCTGCATCAGTGAATCGGCCAAC

M41-MCS-fow: CTAGACTAGTGTTTAAACCGGACCGGGGGGGGGGTT-

AAGGGGGGGGGG

FIG. 35BBBB

M41-MCS-rev: CTAGCCCCCCCCCCCTTAAGCCCCCCCCGGTCCGGT-

TTAAACACTAGT

M41-fow: CTAGACTAGTGTTTAAACCGGACCGGGGGGGGGGCTTAA-

GGGGGGGGGGG

M41-rev: CCCCCCTTAAGTGGGCTGCAAAACAAAACGGCCTCC-

TGTCAGGAAGCCGCTTTTATCGGGTAGCCTCACTGCCCGCTTTCC

M41-A2: GTTGTTGTGCCACGCGGTTAGGAATGTAATTCAGCTCCGC

M41-B1: AACCGCGTGGCACAACAAC

M41-B2: CTTCGTTCTACCATCGACACGACCACGCTGGCACCCAGTTG

M41-C1: GTGTCGATGGTAGAACGAAG

M41-CII: CCACAGCAATAGCATCCTGGTCATCCAGCGGATAGTT-

AATAATCAGCCCACTGACACGTTGCGCGAG

M41-DI: GACCAGGATGCTATTGCTGTGG

M41-DII: CAGCGCGATTTGCTGGTGGCCCAATGCGACCAGATGC

M41-EI: CACCAGCAAATCGCGCTG

M41-EII: CCCGGACTCGGTAATGGCACGCATTGCGCCCAGCGCC

M41-FI: GCCATTACCGAGTCCGGG

M42: synthesis

Eco-H5-Hind-fow: AATTCCACCATCATCACCATTGACGTCTA

Eco-H5-Hind-rev: AGCTTAGACGTCAATGGTGATGGTGG

FIG. 35CCCC

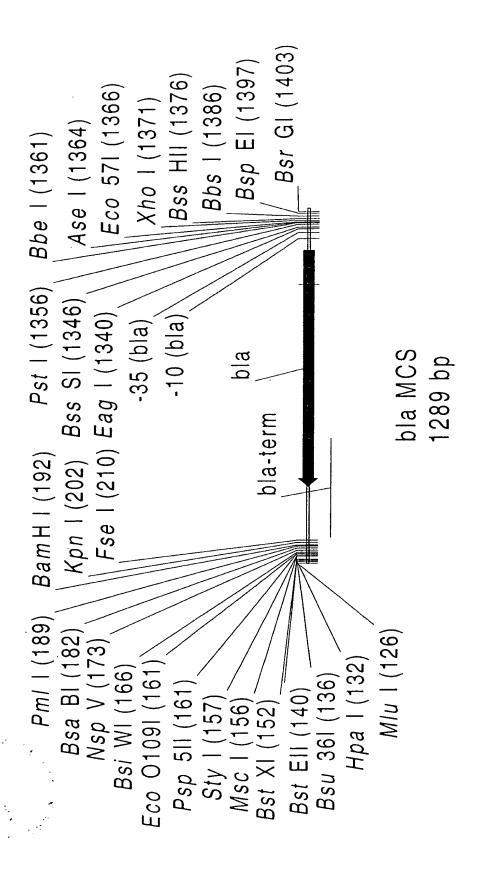


FIG. 36A

|     |                          |                                  |                          | Psp5II                         |                              |  |
|-----|--------------------------|----------------------------------|--------------------------|--------------------------------|------------------------------|--|
|     |                          |                                  |                          | Ecol109I                       |                              |  |
|     | ~~~~~<br>HpaI            | BSTEII                           | Msc                      | I I                            | BsiwI NspV                   |  |
| 126 | CGCGTTAACC               | C TCAGGTGACC<br>G AGTCCACTGG     | AAGCCCCTGG<br>TTCGGGGACC | GG CCAAGGTCCC<br>CC GGTTCCAGGG | c gracgricga<br>c cargcaager |  |
|     |                          | PmlI                             |                          |                                |                              |  |
|     | NspVBsaBI                |                                  | KpnI                     |                                |                              |  |
| 176 | AGATTACCAT<br>TCTAATGGTA | CAT CACGTGGATC<br>GTA GTGCACCTAG | CGGTACCAGG               | 92299<br>29922                 | TCAAAAAGGA<br>AGTTTTTCCT     |  |
| 226 | TCTCAAGAAG<br>AGAGTTCTTC | G ATCCTTTGAT<br>C TAGGAAACTA     | CTTTTCTACG<br>GAAAAGATGC | GGGTCTGACG                     | CTCAGTGGAA<br>GAGTCACCTT     |  |
| 276 | CGAAAACTCA<br>GCTTTTGAGT | A CGTTAAGGGA<br>T GCAATTCCCT     | TTTTGGTCAT<br>AAAACCAGTA | GAGATTATCA<br>CTCTAATAGT       | AAAAGGATCT<br>TTTTCCTAGA     |  |

FIG. 36B

| CTACAGGCAT                | GTTGCCATTG               | GCGCAACGTT               | TTAATAGTTT               | AGTTCGCCAG               | 9 2 9 |
|---------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-------|
| GATGTCCGTA                | CAACGGTAAC               | CGCGTTGCAA               | AATTATCAAA               | TCAAGCGGTC               |       |
| TAGAGTAAGT                | GCCGGGAAGC               | ATTAACTGTT               | CATCCAGTCT               | TATCCGCCTC               | 929   |
| ATCTCATTCA                | CGGCCCTTCG               | TAATTGACAA               | GTAGGTCAGA               | ATAGGCGGAG               |       |
| CCTGCAACTT<br>GGACGTTGAA  | CAGAAĞTGGT<br>GTCTTCACCA | GGGCCGAGCG               | CCAGCCGGAA<br>GGTCGGCCTT | AATAAACCAG<br>TTATTTGGTC | 576   |
| ATTTATCAGC<br>TAAATAGTCG  | CCGGCTCCAG<br>GGCCGAGGTC | CCCACGCTCA<br>GGGTGCGAGT | TACCGCGAGA               | GCTGCAATGA               | 526   |
| TGGCCCCAGT<br>ACCGGGGGTCA | GCTTACCATC<br>CGAATGGTAG | ATACGGGAGG<br>TATGCCCTCC | GATAACTACG<br>CTATTGATGC | CCGTCGTGTA               | 476   |
| GCCTGACTCC<br>CGGACTGAGG  | ATCCATAGTT<br>TAGGTATCAA | TATTTCGTTC               | GCGATCTGTC<br>CGCTAGACAG | ACCTATCTCA<br>TGGATAGAGT | 426   |
| TCAGTGAGGC                | CAATGCTTAA               | TGACAGTTAC               | AAACTTGGTC               | ATATATGAGT               | 376   |
| AGTCACTCCG                | GTTACGAATT               | ACTGTCAATG               | TTTGAACCAG               | TATATACTCA               |       |
| AATCTAAAGT                | GTTTTAAATC               | TAAAAATGAA               | CCTTTTAAAT               | TCACCTAGAT               | 326   |
| TTAGATTTCA                | CAAAATTTAG               | ATTTTTACTT               | GGAAAATTTA               | AGTGGATCTA               |       |

FIG. 36C

| GTTCTTCGGG GCGAAAACTC TCAAGGATCT TACCGCTGTT GAGATCCAGT<br>CAAGAAGCCC CGCTTTTGAG AGTTCCTAGA ATGGCGACAA CTCTAGGTCA | 1076  |
|------------------------------------------------------------------------------------------------------------------|-------|
| TAATACCGCG CCACATAGCA GAACTTTAAA AGTGCTCATC ATTGGAAAAC<br>ATTATGGCGC GGTGTATCGT CTTGAAATTT TCACGAGTAG TAACCTTTTG | 1026  |
| GAATAGTGTA TGCGGCGACC GAGTTGCTCT TGCCCGGCGT CAATACGGGA<br>CTTATCACAT ACGCCGCTGG CTCAACGAGA ACGGGCCGCA GTTATGCCCT | 976   |
| CCGTAAGATG CTTTTCTGTG ACTGGTGAGT ACTCAACCAA GTCATTCTGA<br>GGCATTCTAC GAAAAGACAC TGACCACTCA TGAGTTGGTT CAGTAAGACT | 926   |
| ATCACTCATG GTTATGGCAG CACTGCATAA TTCTCTTACT GTCATGCCAT<br>TAGTGAGTAC CAATACCGTC GTGACGTATT AAGAGAATGA CAGTACGGTA | 876   |
| AGCTCCTTCG GTCCTCCGAT CGTTGTCAGA AGTAAGTTGG CCGCAGTGTT<br>TCGAGGAAGC CAGGAGGCTA GCAACAGTCT TCATTCAACC GGCGTCACAA | 8 2 6 |
| AACGATCAAG GCGAGTTACA TGATCCCCCA TGTTGTGCAA AAAAGCGGTT<br>TTGCTAGTTC CGCTCAATGT ACTAGGGGGT ACAACACGTT TTTTCGCCAA | 776   |
| CGTGGTGTCA CGCTCGTCGT TTGGTATGGC TTCATTCAGC TCCGGTTCCC<br>GCACCACAGT GCGAGCAGCA AACCATACCG AAGTAAGTCG AGGCCAAGGG | 726   |

FIG. 36D

|                          | \<br>H                             | BspEI BsrGI              |                                   | BssHII                   |      |
|--------------------------|------------------------------------|--------------------------|-----------------------------------|--------------------------|------|
| ATGGCTCGAG               | GCGCCA                             |                          | OO                                | ATTTGAATGT<br>TAAACTTACA | 1326 |
| I BssHII                 | Bbel Asel                          | BssSI                    | EagI                              |                          |      |
| XhoI                     |                                    | PstI                     |                                   |                          |      |
| GCGGATACAT<br>CGCCTATGTA | TGTCTCATGA<br>ACAGAGTACT           | TCAGGGTTAT<br>AGTCCCAATA | GAAGCATTTA<br>CTTCGTAAAT          | CAATATTATT<br>GTTATAATAA | 1276 |
| CTTCCTTTTT<br>GAAGGAAAAA | TACTCATACT<br>ATGAGTATGA           | AAATGTTGAA<br>TTTACAACTT | GGCGACACGG<br>CCGCTGTGCC          | AGGGAATAAG<br>TCCCTTATTC | 1226 |
| GCCGCAAAAA<br>CGGCGTTTTT | AAGGCAAAAT<br>TTCCGTTTTA           | CAAAAACAGG<br>GTTTTTGTCC | TCTGGGTGAG<br>AGACCCACTC          | CACCAGCGTT<br>GTGGTCGCAA | 1176 |
| CTTTTACTTT<br>GAAAATGAAA | TCTTCAGCAT<br>AGAAGTCGTA<br>Eco57I | ACCCAACTGA<br>TGGGTTGACT | CCACTCGTGC<br>GGTGAGCACG<br>BSSSI | TCGATGTAAC<br>AGCTACATTG | 1126 |

F/G. 36E

CGCGCTTCAG CGCTTTGTCT TCCGGATGTA CATGAAATT GCGCGAAGTC GCGAAACAGA AGGCCTACAT GTACTTTAA Eco571 Bbs1 1376

F/G. 36F

O\_K3L\_5 5'- G C C T G C A A G C G G A A G A C

BbsI

E D

Vk1 & Vk3 5'- G C C C T G C A A G C G G A A G A C

Vk2 5'- G C C T G C A A G C G G A A G A C

E D

Vk4 5'- G C C C T G C A A G C G G A A G A C

FIG. 37A

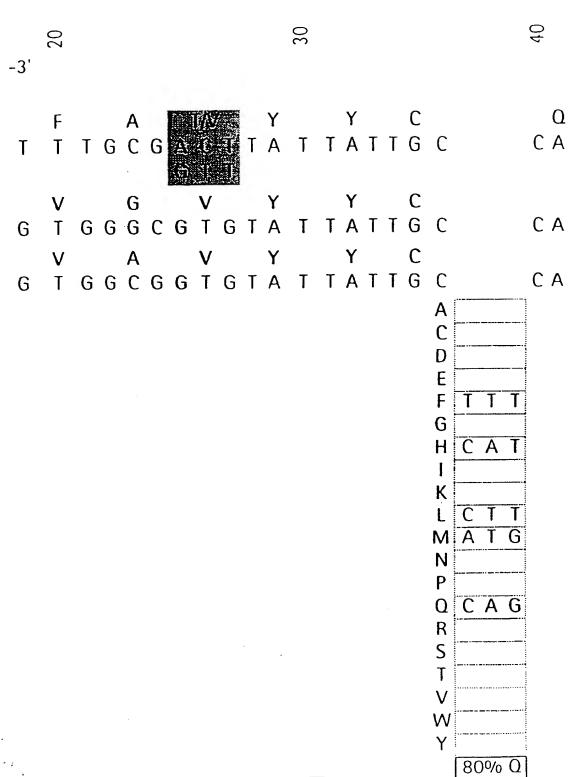


FIG. 37B

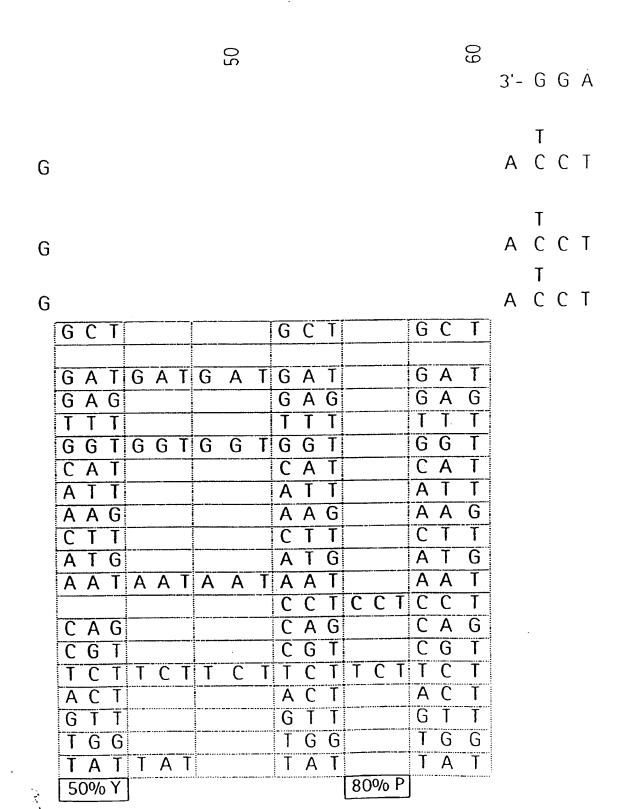


FIG. 37C

FIG. 37D

E D E A D
5'- C C T G C A A G C G G A A G A G C G G A T T -

FIG. 38A

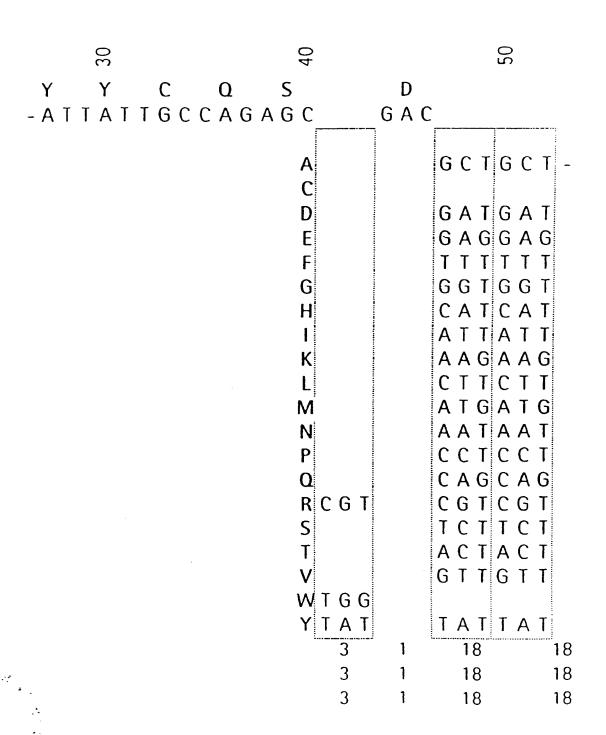
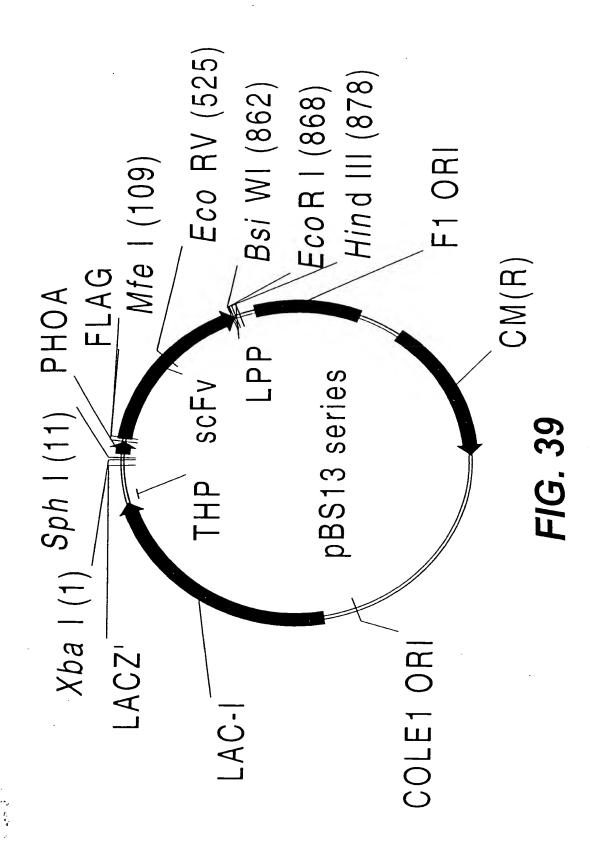


FIG. 38B

|     |     |            |       |     |     | G   |              | G             |            | G   |   | •   | T   |   | K |     |    | L  |   |
|-----|-----|------------|-------|-----|-----|-----|--------------|---------------|------------|-----|---|-----|-----|---|---|-----|----|----|---|
|     |     |            |       |     |     | G G | $\mathbf{C}$ | G G           | $C \in$    | 6 G | C | Α ( | C G | Α | Α | G · | Γ. | TA | 1 |
|     |     | gap        | gap   |     |     |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| - G | CT  | GCT        | GCT   | G C | T   |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
|     |     |            |       |     |     |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| G   | AT  | GAT        | GAT   | G A | \T  |     |              |               |            | •   |   |     |     |   |   |     |    |    |   |
| G   | A G | GAG        | G A G | G A | G   | •   |              |               |            |     |   |     |     |   | ٠ |     |    |    |   |
| T   | TT  | TTT        | TTT   | TT  | T   |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| G   | G T | GGT        | GGT   | GG  | iT  |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| C   | A T | CAT        | CAT   | C A | \ T |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| 1., | •   |            | ATT   |     |     |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
|     |     |            | AAG   | •   |     | 1   |              |               |            |     |   |     |     |   |   |     |    |    |   |
|     | -   | i          | CTT   | 1   |     | 1   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| • • | -   | •          | ATG   | 1   |     | 1   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| 1.  |     |            | AAT   | 1   |     | 1   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| _   | -   | <u>:</u>   | CCT   | •   |     | i   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| •   |     | ;          | CAG   | 1   |     | 1   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| ; - |     |            | CGT   | 1   |     | •   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| 1   |     |            | TCT   | į   |     |     |              |               | ٠          |     |   |     |     |   |   |     |    |    |   |
| • 1 |     |            | ACT   | :   |     |     |              |               |            |     |   |     |     |   |   |     |    |    |   |
| G   |     | $G \cap I$ | GTI   | 1   |     | i   |              |               |            |     |   |     |     |   |   |     |    |    |   |
| -   |     |            |       |     | 3 G | i   |              | _ 1_ 11       | : <b>.</b> |     |   |     |     |   |   |     |    |    |   |
|     |     | IAI        | TAT   |     |     | نـ  |              | abil<br>or. 7 | •          |     |   |     |     |   |   |     |    |    |   |
|     | 18  | 10         |       |     | 9   |     |              | ?E+(          |            |     |   |     |     |   |   |     |    |    |   |
|     | 18  | 18         | 10    |     | 9   |     |              | 3E+(          |            |     |   |     |     |   |   |     |    |    |   |
| 1.  | 18  | 18         | 18    | t   | 9   |     | J.UB         | 3E+(          | JØ         |     |   |     |     |   |   |     |    |    |   |

FIG. 38C

FIG. 38D



|              | 0   |     |     |     | <br>_0 | 9   | 9   |
|--------------|-----|-----|-----|-----|--------|-----|-----|
| <del>ب</del> | 60% | 36% | 45% | 830 | 450    | 47% | 510 |
| 77           | 61% | 39% | 36% | 71% | 33%    | 46% | 20% |
| 71           | %06 | 47% | 37% | 80% | 45%    | 54% | 45% |
| К4           | 42% | 48% | 49% | 61% | 44%    | 67% | 47% |
| $\Sigma$     | 52% | %99 | 46% | 76% | 51%    | 46% | 54% |
| 3            | 58% | 48% | 57% | 67% | 52%    | 49% | 58% |
| 7            | 61% | 39% | 47% | 85% | %69    | 49% | %06 |
| % soluble    | H1A | H1B | H2  | H3  | H4     | HS  | 9H  |

| Total amount     | - 5          | 2    | 5    | 7.5      | 1,   | 3.5  | 12   |
|------------------|--------------|------|------|----------|------|------|------|
| compared to H3K2 | <del>-</del> | 2    | 2    | <b>ታ</b> |      | 7.7  | 2    |
| H1A              | 289%         | 94%  |      | 272%     |      | 150% | 78%  |
| H18              | 219%         | 122% |      | 139%     |      | 158% | 101% |
| H2               | 186%         | 223% | 208% | 182%     | 126% | %09  | 97%  |
| H3               | 20%          |      |      | 54%      |      | 130% | 47%  |
| H4               | 37%          | 55%  |      | 77%      |      | 107% | 251% |
| H5               | 98%          | 201% |      | 83%      |      | 128% | 115% |
| 9H               | 65%          | 117% |      | 109%     |      | 215% | 278% |

## F/G. 40A

| Soluble amount   | ,        |      |        | 7          | ) 1      | ,    | ,     |
|------------------|----------|------|--------|------------|----------|------|-------|
| compared to H3K2 | <u>~</u> | 7    | χ<br>Σ | Κ <b>4</b> | K4 VI VZ | 77   | کہ    |
| H1A              | 191%     | 88%  | 121%   | 122%       | 26%      | 211% | 0/09/ |
| H18              | 124%     | 95%  | 83%    | 107%       | 79%      | 142% | 29%   |
| H2               | 126%     | 204% | 139%   | 130%       | %99      | 20%  | 0/00/ |
| H3               | 63%      | ı    | 81%    | 49%        | %69      | 143% | 61%   |
| H4               | 40%      | 47%  | 49%    | 54%        | 95%      | 55%  | 125%  |
| HS               | %69      | 158% | 116%   | 80%        | 72%      | 84%  | 84%   |
| 9H               | 85%      | 122% | 87%    | 77%        | 162%     | 162% | 212%  |
|                  | McPC     |      |        |            |          |      |       |
| soluble          | 38%      |      |        |            |          |      |       |
| %H3k2 total      | 117%     |      |        |            |          |      |       |
| %H3k2 soluble    | 69%      |      |        |            |          |      |       |

## FIG. 40B